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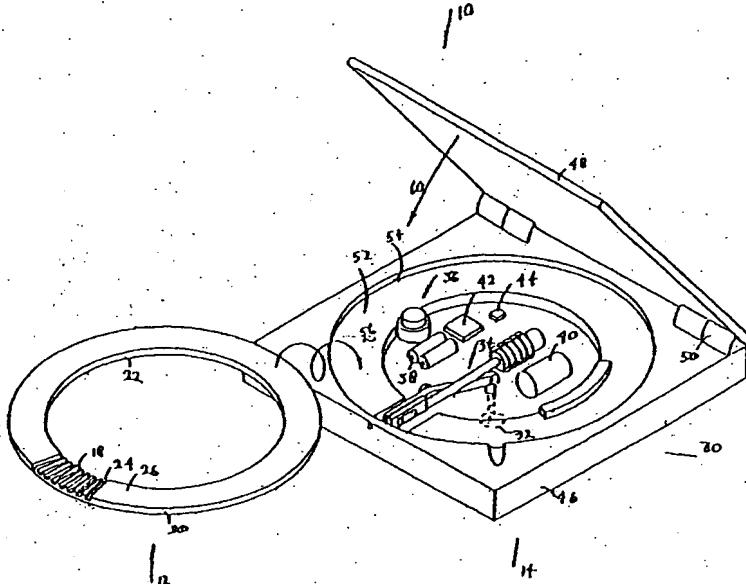
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(54) Title: METHOD AND APPARATUS FOR MEASURING ANALYTES



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(57) Abstract: A device comprises a cartridge (12) and a plurality of analyte detecting members (18) mounted on said cartridge. The cartridge may have a radial disc shape. The analyte detecting members may be a three-electrode system wherein only a working electrode is covered with a glucose oxidase. In one embodiment, the device may also include a fluid spreader (28) positioned over at least a portion of said analyte detecting member to urge fluid toward one of the detecting members. A plurality of analyte detecting members may be used. Each analyte detecting member may be a low volume device.



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METHOD AND APPARATUS FOR MEASURING ANALYTES

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BACKGROUND OF THE INVENTION

Lancing devices are known in the medical health-care products industry for piercing the skin to produce blood for analysis. Typically, a drop of blood for this type of analysis is obtained by making a small incision in the fingertip, creating a small wound, 10 which generates a small blood droplet on the surface of the skin.

Early methods of lancing included piercing or slicing the skin with a needle or razor. Current methods utilize lancing devices that contain a multitude of spring, cam and mass actuators to drive the lancet. These include cantilever springs, diaphragms, coil springs, as well as gravity plumbs used to drive the lancet. The device may be held 15 against the skin and mechanically triggered to ballistically launch the lancet.

Unfortunately, the pain associated with each lancing event using known technology discourages patients from testing. In addition to vibratory stimulation of the skin as the driver impacts the end of a launcher stop, known spring based devices have the possibility of firing lancets that harmonically oscillate against the patient tissue, causing multiple 20 strikes due to recoil. This recoil and multiple strikes of the lancet is one major impediment to patient compliance with a structured glucose monitoring regime.

Another impediment to patient compliance is the lack of spontaneous blood flow generated by known lancing technology. In addition to the pain as discussed above, a patient may need more than one lancing event to obtain a blood sample since spontaneous 25 blood generation is unreliable using known lancing technology. Thus the pain is multiplied by the number of attempts required by a patient to successfully generate spontaneous blood flow. Different skin thickness may yield different results in terms of pain perception, blood yield and success rate of obtaining blood between different users of the lancing device. Known devices poorly account for these skin thickness variations.

30 A still further impediment to improved compliance with glucose monitoring are the many steps and inconvenience associated with each lancing event. Many diabetic patients that are insulin dependent may need to self-test for blood glucose levels five to six times daily. The large number of steps required in traditional methods of glucose

testing, ranging from lancing, to milking of blood, applying blood to a test strip, and getting the measurements from the test strip, discourages many diabetic patients from testing their blood glucose levels as often as recommended. Older patients and those with deteriorating motor skills encounter difficulty loading lancets into launcher devices,

5 transferring blood onto a test strip, or inserting thin test strips into slots on glucose measurement meters. Additionally, the wound channel left on the patient by known systems may also be of a size that discourages those who are active with their hands or who are worried about healing of those wound channels from testing their glucose levels.

Still further, the inconvenience of having to carry around a large number of individual test

10 strips encumbers the users of conventional test equipment.

SUMMARY OF THE INVENTION

The present invention provides solutions for at least some of the drawbacks discussed above. Specifically, some embodiments of the present invention provide a multiple lancet solution to measuring analyte levels in the body. The invention may use a high density design, with regards to the number of penetrating members in a cartridge or number of analyte detecting members on a cartridge. The present invention may provide an indicator of the point of impact of a lancet or penetrating member used to sample fluid from tissue. At least some of these and other objectives described herein will be met by

15 embodiments of the present invention.

In one embodiment of the present invention, a device is provided for use with a body fluid sampling device for extracting bodily fluid from an anatomical feature. The device comprises a cartridge having a plurality of cavities. The device may include a plurality of penetrating members each at least partially contained in the cavities of the

25 cartridge wherein the penetrating members are slidably movable to extend outward from openings on the cartridge to penetrate tissue. The device may also include a plurality of analyte detecting members and a plurality of chambers. Each chamber may be associated with one of the cavities, the chambers positioned along an outer periphery of the cartridge, wherein at least one of the analyte detecting members forms a portion of one

30 wall of one of the plurality of chambers.

In one embodiment, the device may also include a fluid spreader positioned over at least a portion of the analyte detecting member to urge fluid toward one of the detecting members. The penetrating members may each have a tip, wherein at least one

tip has a starting position in the chamber. The analyte detecting members may be electrochemical. In one embodiment, at least one of the chambers includes an opening on one of its surfaces, wherein one of the analyte detecting members is visible through the opening.

- 5 In another embodiment, the present invention provides a device for use with a body fluid sampling device for extracting bodily fluid from an anatomical feature. The device comprises a cartridge having a plurality of sample chambers and a plurality of penetrating members each at least partially contained in the sample chambers of the single cartridge wherein the penetrating members are slidably movable to extend outward
10 from openings on the cartridge to penetrate tissue. A plurality of analyte detecting members may be included. The chambers may be positioned substantially adjacent an outer periphery of the cartridge, wherein at least one of the analyte detecting members forms a portion of one wall of one of the plurality of sample chambers.

The present invention may be directed at providing systems, methods, and devices
15 for using multiple sensors to measure an analyte in a body fluid. At least some embodiments will do so using electrochemical analyte measuring techniques. In one embodiment, the sensors are low volume sensors each using less than about 500 nanoliters to obtain an analyte measurement.

The present invention is directed at providing multiple sensors having
20 sensitivities over multiple concentration ranges. Additionally, these sensors may have low body fluid volume requirements, allowing for multiple sensors to be used at one time using spontaneous blood available from a standard lancet wound or prick on a patient's finger or other tissue site.

Microfluidics may be used to channel blood to some or all of these sensors. In
25 one embodiment, these sensors may be a sensor using a potentiometric glucose measurement technique.

Nanowires may be provided for these sensors. In one embodiment of the present invention, these wires may be in the size of 100 nanometers by 20 nanometer size (0.1 micrometer). This may be made into a sensor design with electronics to monitor glucose.
30 This could be designed into a sensor of about 1 micrometer x 1 micrometer (1-10 nanoliters blood requirement). An array of sensors could be made. Some number of sensors say 50 each may be devoted for each concentration range for statistical advantage. This gains by eliminating noise issues that may be associated in some sensors, but not

seen in others. The accuracy gains by the square root of the number of sides. In some embodiments, several areas each having multiple sensors may be dedicated to each concentration range.

In one aspect of the present invention, a glucose sensor is provided that uses a 5 potentiometric technique to measure glucose levels in blood or body fluid volumes of less than about 500 nanoliters. Multiple glucose sensors may be added to improve accuracy.

In another embodiment, the device may comprise a cassette having a sample exposure region and a nanowire. The detection of an analyte in a sample in the sample exposure region may occur while the cassette is disconnected to a detector apparatus, 10 allowing samples to be gathered at one site, and detected at another. The cassette may be operatively connectable to a detector apparatus able to determine a property associated with the nanowire. As used herein, a device is "operatively connectable" when it has the ability to attach and interact with another apparatus. In other embodiments, the detection apparatus is fully integrated with sample collector having the sample exposure region.

In another embodiment, one or more nanowires may be positioned in a 15 microfluidic channel. One or more different nanowires may cross the same microchannel at different positions to detect a different analyte or to measure flow rate of the same analyte. In another embodiment, one or more nanowires positioned in a microfluidic channel may form one of a plurality of analytic elements in a micro needle probe or a dip 20 and read probe. The micro needle probe is implantable and capable of detecting several analytes simultaneously in real time. In another embodiment, one or more nanowires positioned in a microfluidic channel may form one of the analytic elements in a microarray for a cassette or a lab on a chip device. Those skilled in the art would know such cassette or lab on a chip device will be in particular suitable for high throughout 25 chemical analysis and combinational drug discovery. Moreover, the associated method of using the nanoscale sensor is fast and simple, in that it does not require labeling as in other sensing techniques. The ability to include multiple nanowires in one nanoscale sensor, also allows for the simultaneous detection of different analytes suspected of being present in a single sample. For example, a nanoscale pH sensor may include a plurality of 30 nanoscale wires that each detects different pH levels.

A further understanding of the nature and advantages of the invention will become apparent by reference to the remaining portions of the specification and drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a perspective view illustrating a system, according to an embodiment for use in piercing skin to obtain a blood sample;

5 Figure 2 is a plan view of a portion of a replaceable penetrating member cartridge forming part of the system;

Figure 3 is a cross-sectional end view on 3-3 in Figure 2;

Figure 4 is a cross-sectional end view on 4-4 in Figure 2;

10 Figure 5 is a perspective view of an apparatus forming part of the system and used for manipulating components of the cartridge, illustrating pivoting of a penetrating member accelerator in a downward direction;

Figure 6A is a view similar to Figure 5, illustrating how the cartridge is rotated or advanced;

Figure 6B is a cross-sectional side view illustrating how the penetrating member accelerator allows for the cartridge to be advanced;

15 Figure 7A and 7B are views similar to Figures 6A and 6B, respectively, illustrating pivoting of the penetrating member accelerator in an opposite direction to engage with a select one of the penetrating members in the cartridge;

20 Figures 8A and 8B are views similar to Figures 7A and 7B, respectively, illustrating how the penetrating member accelerator moves the selected penetrating member to pierce skin;

Figures 9A and 9B are views similar to Figures 8A and 8B, respectively, illustrating how the penetrating member accelerator returns the penetrating member to its original position;

25 Figure 10 is a block diagram illustrating functional components of the apparatus; and

Figure 11 is an end view illustrating a cartridge according to an optional embodiment that allows for better adhesion of sterilization barriers.

Figure 12 is a cross-sectional view of an embodiment having features of the invention;

30 Figure 13 is a cross-sectional view of an embodiment having features of the invention in operation.

Figure 14 is a cross-sectional view illustrating a low-friction coating applied to one penetrating member contact surface.

Figure 15 is a cross-sectional view illustrating a coating applied to one penetrating member contact surface which increases friction and improves the microscopic contact area between the penetrating member and the penetrating member contact surface.

Figure 16 illustrates a portion of a penetrating member cartridge having an annular configuration with a plurality of radially oriented penetrating member slots and a distal edge of a drive member disposed in one of the penetrating member slots.

Figure 17 is an elevational view in partial longitudinal section of a coated penetrating member in contact with a coated penetrating member contact surface.

Figure 18 illustrates an embodiment of a lancing device having features of the invention.

Figure 19 is a perspective view of a portion of a penetrating member cartridge base plate having a plurality of penetrating member slots and drive member guide slots disposed radially inward of and aligned with the penetrating member slots.

Figures 20-22 illustrate a penetrating member cartridge in section, a drive member, a penetrating member and the tip of a patient's finger during three sequential phases of a lancing cycle.

Figure 23 illustrates an embodiment of a penetrating member cartridge having features of the invention.

Figure 24 is an exploded view of a portion of the penetrating member cartridge of Figure 12.

Figures 25 and 26 illustrate a multiple layer sterility barrier disposed over a penetrating member slot being penetrated by the distal end of a penetrating member during a lancing cycle.

Figures 27 and 28 illustrate an embodiment of a drive member coupled to a driver wherein the drive member includes a cutting member having a sharpened edge which is configured to cut through a sterility barrier of a penetrating member slot during a lancing cycle in order for the drive member to make contact with the penetrating member.

Figures 29 and 30 illustrate an embodiment of a penetrating member slot in longitudinal section having a ramped portion disposed at a distal end of the penetrating member slot and a drive member with a cutting edge at a distal end thereof for cutting through a sterility barrier during a lancing cycle.

Figures 31-34 illustrate drive member slots in a penetrating member cartridge wherein at least a portion of the drive member slots have a tapered opening which is

larger in transverse dimension at the top of the drive member slot than at the bottom of the drive member slot.

Figures 35-37 illustrate an embodiment of a penetrating member cartridge and penetrating member drive member wherein the penetrating member drive member has a 5 contoured jaws configured to grip a penetrating member shaft.

Figures 38 and 39 show a portion of a lancing device having a lid that can be opened to expose a penetrating member cartridge cavity for removal of a used penetrating member cartridge and insertion of a new penetrating member cartridge.

Figures 40 and 41 illustrate a penetrating member cartridge that has penetrating 10 member slots on both sides.

Figures 42-44 illustrate end and perspective views of a penetrating member cartridge having a plurality of penetrating member slots formed from a corrugated surface of the penetrating member cartridge.

Figures 45-48 illustrate embodiments of a penetrating member and drive member 15 wherein the penetrating member has a slotted shaft and the drive member has a protuberance configured to mate with the slot in the penetrating member shaft.

Figure 49 is a perspective view of a cartridge according to the present invention.

Figures 50 and 51 show close-ups of outer peripheries various cartridges.

Figure 52 is a perspective view of an underside of a cartridge.

20 Figure 53A shows a top down view of a cartridge and the punch and pusher devices.

Figure 53B is a perspective view of one embodiment of a punch plate.

Figures 54A-54G show a sequence of motion for the punch plate, the cartridge, and the cartridge pusher.

25 Figures 55A-55B show cross-sections of the system according to the present invention.

Figure 56A shows a perspective view of the system according to the present invention.

Figures 56B-56D are cut-away views showing mechanisms within the present 30 invention.

Figures 57-65B show optional embodiments according to the present invention.

Figure 66-68 shows a still further embodiment of a cartridge according to the present invention.

Figures 69A-69L show the sequence of motions associated with an optional embodiment of a cartridge according to the present invention.

Figure 70-72 show views of a sample modules used with still further embodiments of a cartridge according to the present invention.

5 Figure 73 shows a cartridge with a sterility barrier and an analyte detecting member layer.

Figure 74-78 show still further embodiments of analyte detecting members coupled to a cartridge.

10 Figures 79-84 show optional configurations for a cartridge for use with the present invention.

Figure 85 shows a see-through view of one embodiment of a system according to the present invention.

Figure 86 is a schematic of an optional embodiment of a system according to the present invention.

15 Figures 87A-87B show still further embodiments of cartridges according to the present invention.

Figure 88 shows a cartridge having an array of analyte detecting members.

Figures 89-90 show embodiments of illumination systems for use with the present invention.

20 Figures 91-96 show further embodiments using optical methods for analyte detection.

Figure 97 shows a chart of varying penetrating member velocity in different parts of the tissue.

25 Figure 98 shows a cross-sectional view of a light source used with aiming the driver.

Figure 99 and 100 show cross-sectional views of housings having a light source used with aiming the driver.

Figures 101 and 102 show a housing wherein a portion is made of a clear material.

30 Figure 103 shows a cartridge, sterility barrier, and a substrate according to the present invention.

Figures 104-105 show perspective views of one embodiment of the present invention.

Figures 106-107 show perspective views of an underside of one embodiment of the present invention.

Figures 108 and 109 show a top view and bottom view of a further embodiment of a cartridge according to the present invention.

5 Figures 108 and 109 show a top perspective view and a bottom perspective view of a further embodiment of a cartridge according to the present invention.

Figure 112 shows additional embodiments for use with the present invention.

Figures 113-115 show various views of a still further embodiment of a cartridge and analyte detecting members according to the present invention.

10 Figures 116 and 117 show a top view and bottom view of a further embodiment of a cartridge according to the present invention.

Figures 118-119 shows additional embodiments for use with the present invention.

15 Figure 120 is a top down view of a cartridge using a fluid spreader over the analyte detecting member.

Figures 121-123 are perspective views of further embodiments of a cartridge according to the present invention.

Figures 124-125 show kits according to the present invention.

Figures 126-128 are graphs showing analyte detecting member sensitivities.

20 Figure 129 shows an embodiment of a cartridge having a plurality of analyte detecting members.

Figures 130-132 show various configurations of arrays of analyte detecting members.

Figures 133A-133B show nanowire manufacturing techniques.

25 Figure 134 shows an array.

Figure 135 shows the interaction of moieties to be detected and an FET.

Figure 136 shows another embodiment of an analyte detecting member.

Figure 137 shows on method for depositing materials on an electrode.

Figures 138 shows a cartridge suitable for housing a single penetrating member and 30 having a plurality of analyte detecting members.

Figures 139-140 show top down views of the cartridge and the analyte detecting member.

Figure 141 shows a view of the underside of the cartridge and the analyte detecting member.

Figure 142 shows a cross-section of one embodiment of the analyte detecting member.

5 Figure 143 shows an exploded view of one embodiment of the analyte detecting member.

Figures 144-147 show various views of an embodiment of a radial cartridge having a plurality of analyte detecting members.

10 Figure 148 shows a close-up view of one embodiment of contact pads used in the present invention.

Figures 149-150 show various embodiments of a radial cartridge having a plurality of analyte detecting members.

Figure 151 shows one embodiment of a radial cartridge in a housing.

15 Figure 152-153 show still further embodiments of a cartridge having a plurality of analyte detecting members.

DESCRIPTION OF THE SPECIFIC EMBODIMENTS

The present invention provides a multiple analyte detecting member solution for 20 body fluid sampling. Specifically, some embodiments of the present invention provide a multiple analyte detecting member and multiple lancet solution to measuring analyte levels in the body. The invention may use a high density design. It may use lancets of smaller size, such as but not limited to diameter or length, than known lancets. The device may be used for multiple lancing events without having to remove a disposable 25 from the device. The invention may provide improved sensing capabilities. At least some of these and other objectives described herein will be met by embodiments of the present invention.

It is to be understood that both the foregoing general description and the following 30 detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed. It must be noted that, as used in the specification and the appended claims, the singular forms "a", "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a material" may include mixtures of materials, reference to "a chamber" may include multiple chambers, and the

like. References cited herein are hereby incorporated by reference in their entirety, except to the extent that they conflict with teachings explicitly set forth in this specification.

In this specification and in the claims which follow, reference will be made to a number of terms which shall be defined to have the following meanings:

5 "Optional" or "optionally" means that the subsequently described circumstance may or may not occur, so that the description includes instances where the circumstance occurs and instances where it does not. For example, if a device optionally contains a feature for analyzing a blood sample, this means that the analysis feature may or may not be present, and, thus, the description includes structures wherein a device possesses the
10 analysis feature and structures wherein the analysis feature is not present.

"Analyte detecting member" refers to any use, singly or in combination, of chemical test reagents and methods, electrical test circuits and methods, physical test components and methods, optical test components and methods, and biological test reagents and methods to yield information about a blood sample. Some of these methods
15 are well known in the art and may be based on teachings of, e.g. Tietz Textbook of Clinical Chemistry, 3d Ed., Sec. V, pp. 776-78 (Burtis & Ashwood, Eds., W.B. Saunders Company, Philadelphia, 1999); U.S. Pat. No. 5,997,817 to Chrismore et al. (Dec. 7, 1999); U.S. Pat. No. 5,059,394 to Phillips et al. (Oct. 22, 1991); U.S. Pat. No. 5,001,054
20 to Wagner et al. (Mar. 19, 1991); and U.S. Pat. No. 4,392,933 to Nakamura et al. (July 12, 1983), the teachings of which are hereby incorporated by reference, as well as others.

Analyte detecting member may include tests in the sample test chamber that test electrochemical properties of the blood, or they may include optical means for sensing optical properties of the blood (e.g. oxygen saturation level), or they may include biochemical reagents (e.g. antibodies) to sense properties (e.g. presence of antigens) of the blood. The analyte detecting member may comprise biosensing or reagent material that will react with an analyte in blood (e.g. glucose) or other body fluid so that an appropriate signal correlating with the presence of the analyte is generated and can be read by the reader apparatus. By way of example and not limitation, analyte detecting member may be "associated with", "mounted within", or "coupled to" a chamber or other
25 structure when the analyte detecting member participates in the function of providing an appropriate signal about the blood sample to the reader device. Analyte detecting member may also include nanowire analyte detecting members as described herein.
30

Analyte detecting member may use any, singly or in combination, potentiometric, coulometric, or other method useful for detection of analyte levels.

Figures 1-11 of the accompanying drawings illustrates one embodiment of a system 10 for piercing tissue to obtain a blood sample. The system 10 may include a 5 replaceable cartridge 12 and an apparatus 14 for removably receiving the cartridge 12 and for manipulating components of the cartridge 12.

Referring jointly to Figures 1 and 2, the cartridge 12 may include a plurality of penetrating members 18. The cartridge 12 may be in the form of a circular disc and has an outer circular surface 20 and an opening forming an inner circular surface 22. A 10 plurality of grooves 24 are formed in a planar surface 26 of the cartridge 12. Each groove 24 is elongated and extends radially out from a center point of the cartridge 12. Each groove 24 is formed through the outer circular surface 20. Although not shown, it should be understood that the grooves 24 are formed over the entire circumference of the planar surface 26. As shown in Figures 3 and 4, each groove 24 is relatively narrow closer to the 15 center point of the cartridge 12 and slightly wider further from the center point. These grooves 24 may be molded into the cartridge 12, machined into the cartridge, forged, pressed, or formed using other methods useful in the manufacture of medical devices.

In the present embodiment, each penetrating member 18 has an elongated body 26 and a sharpened distal end 27 having a sharp tip 30. The penetrating member 18 may 20 have a circular cross-section with a diameter in this embodiment of about 0.315 mm. All outer surfaces of the penetrating member 18 may have the same coefficient of friction. The penetrating member may be, but is not necessarily, a bare lancet. The lancet is "bare", in the sense that no raised formations or molded parts are formed thereon that are complementarily engageable with another structure. Traditional lancets include large 25 plastic molded parts that are used to facilitate engagement. Unfortunately, such attachments add size and cost. In the most basic sense, a bare lancet or bare penetrating member is an elongate wire having sharpened end. If it is of sufficiently small diameter, the tip may be penetrating without having to be sharpened. A bare lancet may be bent and still be considered a bare lancet. The bare lancet in one embodiment may be made of 30 one material.

In the present embodiment, each penetrating member 18 is located in a respective one of the grooves 24. The penetrating members 18 have their sharpened distal ends 27 pointed radially out from the center point of the cartridge 12. A proximal end of each

penetrating member 15 may engage in an interference fit with opposing sides of a respective groove 24 as shown in Figure 3. Other embodiments of the cartridge 12 may not use such an interference fit. As a nonlimiting example, they may use a fracturable adhesive to releasably secure the penetrating member 18 to the cartridge 12. As shown in 5 Figure 4, more distal portions of the penetrating member 18 are not engaged with the opposing sides of the groove 24 due to the larger spacing between the sides.

The cartridge 12 may further include a sterilization barrier 28 attached to the upper surface 26. The sterilization barrier 28 is located over the penetrating members 18 and serves to insulate the penetrating members 18 from external contaminants. The 10 sterilization barrier 28 is made of a material that can easily be broken when an edge of a device applies a force thereto. The sterilization barrier 28 alone or in combination with other barriers may be used to create a sterile environment about at least the tip of the penetrating member prior to lancing or actuation. The sterilization barrier 28 may be made of a variety of materials such as but not limited to metallic foil, aluminum foil, 15 paper, polymeric material, or laminates combining any of the above. Other details of the sterilization barrier are detailed herein.

In the present embodiment, the apparatus 14 may include a housing 30, an initiator button 32, a penetrating member movement subassembly 34, a cartridge advance subassembly 36, batteries 38, a capacitor 40, a microprocessor controller 42, and switches 20 44. The housing 30 may have a lower portion 46 and a lid 48. The lid 48 is secured to the lower portion 46 with a hinge 50. The lower portion 46 may have a recess 52. A circular opening 54 in the lower portion 46 defines an outer boundary of the recess 52 and a level platform 56 of the lower portion 46 defines a base of the recess 52.

In use, the lid 48 of the present embodiment is pivoted into a position as shown in 25 Figure 1. The cartridge 12 is flipped over and positioned in the recess 52. The planar surface 26 rests against the level platform 56 and the circular opening 54 contacts the outer circular surface 20 to prevent movement of the cartridge 12 in a plane thereof. The lid 48 is then pivoted in a direction 60 and closes the cartridge 12.

Referring to the embodiment shown in Figure 5, the penetrating member 30 movement subassembly 34 includes a lever 62, a penetrating member accelerator 64, a linear actuator 66, and a spring 68. Other suitable actuators including but not limited to rotary actuators are described in commonly assigned, copending U.S. Patent Application Ser. No. 10/127,395 (Attorney Docket No. 38187-2551) filed April 19, 2002. The lever

- 62 may be pivotably secured to the lower portion 46. The button 32 is located in an accessible position external of the lower portion 46 and is connected by a shaft 70 through the lower portion 46 to one end of the lever 62. The penetrating member accelerator 64 is mounted to an opposing end of the lever 62. A user depresses the button 32 in an upward direction 66 so that the shaft 70 pivots the end of the lever 62 to which it is connected in an upward direction. The opposing end of the lever pivots in a downward direction 66. The spring 46 is positioned between the button 32 and the base 40 and compresses when the button 32 is depressed to create a force that tends to move the button 32 down and pivot the penetrating member accelerator upward in a direction opposite to the direction 64.

Referring to Figures 6A and 6B in this particular embodiment, the movement of the button into the position shown in Figure 5 also causes contact between a terminal 74 on the shaft 20 with a terminal 70 secured to the lower portion 46. Contact between the terminals 74 and 76 indicates that the button 32 has been fully depressed. With the button 32 depressed, the cartridge 12 can be rotated without interference by the penetrating member actuator 64. To this effect, the cartridge advancer subsystem 36 includes a pinion gear 80 and a stepper motor 82. The stepper motor 82 is secured to the lower portion 46. The pinion gear 80 is secured to the stepper motor 82 and is rotated by the stepper motor 82. Teeth on the pinion gear 80 engage with teeth on the inner circular surface 22 of the cartridge 12. Rotation of the pinion gear 80 causes rotation of the cartridge 12 about the center point thereof. Each time that the terminals 74 and 76 make contact, the stepper motor 82 is operated to rotate the cartridge 12 through a discrete angle equal to an angular spacing from a centerline of one of the penetrating members 18 to a centerline of an adjacent penetrating member. A select penetrating member 18 is so moved over the penetrating member accelerator 64, as shown in Figure 6B. Subsequent depressions of the button 32 will cause rotation of subsequent adjacent penetrating members 18 into a position over the penetrating member accelerator 64.

The user then releases pressure from the button, as shown in Figure 7A. The force created by the spring 68 or other resilient member moves the button 32 in a downward direction 76. The shaft 70 is pivotably secured to the lever 62 so that the shaft 70 moves the end of the lever 62 to which it is connected down. The opposite end of the lever 62 pivots the penetrating member accelerator 64 upward in a direction 80. As shown in Figure 7B, an edge 82 of the penetrating member accelerator 64 breaks through a portion

of the sterilization barrier 28 and comes in to physical contact with a lower side surface of the penetrating member 18.

Referring to Figure 8A, the linear actuator 66 includes separate advancing coils 86A and retracting coils 86B, and a magnetizable slug 90 within the coils 86A and 86B.

5 The coils 86A and 86B are secured to the lower portion of 46, and the slug 90 can move within the coils 86A and 86B. Once the penetrating member accelerator 64 is located in the position shown in Figures 7A and 7B, electric current is provided to the advancing coils 86 only. The current in the advancing coils 86 creates a force in a direction 88 on the slug 90 according to conventional principles relating to electromagnetics.

10 A bearing 91 is secured to the lever and the penetrating member accelerator 64 has a slot 92 over the bearing 91. The slot 92 allows for the movement of the penetrating member accelerator 64 in the direction 88 relative to the lever 62, so that the force created on the slug moves the penetrating member accelerator 64 in the direction 88.

The spring 68 is not entirely relaxed, so that the spring 68, through the lever 62, 15 biases the penetrating member accelerator 64 against the lower side surface of the penetrating member 18 with a force F1. The penetrating member 18 rests against a base 88 of the cartridge 12. An equal and opposing force F2 is created by the base 88 on an upper side surface of the penetrating member 18.

The edge 82 of the penetrating member accelerator 64 has a much higher 20 coefficient of friction than the base 88 of the cartridge 12. The higher coefficient of friction of the edge contributes to a relatively high friction force F3 on the lower side surface of the penetrating member 18. The relatively low coefficient of friction of the base 88 creates a relatively small friction force F4 on the upper side surface of the penetrating member 18. A difference between the force F3 and F4 is a resultant force that 25 accelerates the penetrating member in the direction 88 relative to the cartridge 12. The penetrating member is moved out of the interference fit illustrated in Figure 3. The bare penetrating member 18 is moved without the need for any engagement formations on the penetrating member. Current devices, in contrast, often make use a plastic body molded onto each penetrating member to aid in manipulating the penetrating members.

30 Movement of the penetrating member 18 moves the sharpened end thereof through an opening 90 in a side of the lower portion 46. The sharp end 30 of the penetrating member 18 is thereby moved from a retracted and safe position within the lower portion 46 into a position wherein it extends out of the opening 90. Accelerated, high-speed

movement of the penetrating member is used so that the sharp tip 30 penetrates skin of a person. A blood sample can then be taken from the person, typically for diabetic analysis.

Reference is now made to Figures 9A and 9B. After the penetrating member is accelerated (for example, but not limitation, less than .25 seconds thereafter), the current to the accelerating coils 86A is turned off and the current is provided to the retracting coils 86B. The slug 90 moves in an opposite direction 92 together with the penetrating member accelerator 64. The penetrating member accelerator 64 then returns the used penetrating member into its original position, i.e., the same as shown in Figure 7B.

Subsequent depression of the button as shown in Figure 5 will then cause one 10 repetition of the process described, but with an adjacent sterile penetrating member.

Subsequent sterile penetrating members can so be used until all the penetrating members have been used, i.e., after one complete revolution of the cartridge 12. In this embodiment, a second revolution of the cartridge 12 is disallowed to prevent the use of 15 penetrating members that have been used in a previous revolution and have become contaminated. The user can continue to use the apparatus 14 is by opening 'the lid 48 as shown in Figure 1, removing the used cartridge 12, and replacing the used cartridge with another cartridge. A detector (not shown) detects whenever a cartridge is removed and replaced with another cartridge. Such a detector may be but is not limited to an optical sensor, an electrical contact sensor, a bar code reader, or the like.

Figure 10 illustrates the manner in which the electrical components may be 20 functionally interconnected for the present embodiment. The battery 38 provides power to the capacitor 40 and the controller 42. The terminal 76 is connected to the controller 42 so that the controller recognizes when the button 32 is depressed. The capacitor to provide power (electric potential and current) individually through the switches (such as 25 but not limited to field-effect transistors) to the advancing coils 86A, retracting coils 86B and the stepper motor 82. The switches 44A, B, and C are all under the control of the controller 42. A memory 100 is connected to the controller. A set of instructions is stored in the memory 100 and is readable by the controller 42. Further functioning of the controller 42 in combination with the terminal 76 and the switches 44A, B, and C should 30 be evident from the foregoing description.

Figure 11 illustrates a configuration for another embodiment of a cartridge having penetrating members. The cartridge 112 has a corrugated configuration and a plurality of penetrating members 118 in grooves 124 formed in opposing sides of the cartridge 112.

Sterilization barriers 126 and 128 are attached over the penetrating members 118 at the top and the penetrating members 118 at the bottom, respectively. Such an arrangement provides large surfaces for attachment of the sterilization barriers 126 and 128. All the penetrating members 118 on the one side are used first, whereafter the cartridge 112 is 5 turned over and the penetrating members 118 on the other side are used. Additional aspects of such a cartridge are also discussed in Figures 42-44.

Referring now to Figures 12-13, a friction based method of coupling with and driving bare lancets or bare penetrating members will be described in further detail. Any embodiment of the present invention disclosed herein may be adapted to use these 10 methods. As seen in Figure 12, surface 201 is physically in contact with penetrating member 202. Surface 203 is also physically in contact with penetrating member 202. In the present embodiment of the invention, surface 201 is stainless steel, penetrating member 202 is stainless steel, and surface 203 is polytetrafluoroethylene-coated stainless steel.

Figure 13 illustrates one embodiment of the friction based coupling in use. Normal force 206 may be applied vertically to surface 201, pressing it against penetrating member 202. Penetrating member 202 is thereby pressed against surface 203. Normal force 206 is transmitted through surface 201 and penetrating member 202 to also act between penetrating member 202 and surface 203. Surface 203 is held rigid or stationary 20 with respect to a target of the lancet. Using the classical static friction model, the maximum frictional force between surface 201 and penetrating member 202 is equal to the friction coefficient between surface 201 and penetrating member 202 multiplied by the normal force between surface 201 and penetrating member 202. In this embodiment, the maximum frictional force between surface 203 and penetrating member 202 is equal 25 to the coefficient of friction between the surface 203 and the penetrating member 202 multiplied by the normal force between the surface 203 and the penetrating member 202. Because friction coefficient between surface 203 and penetrating member 202 is less than friction coefficient between surface 201 and penetrating member 202, the interface between surface 201 and penetrating member 202 can develop a higher maximum static 30 friction force than can the interface between surface 203 and penetrating member 202.

Driving force as indicated by arrow 207 is applied to surface 201 perpendicular to normal force 206. The sum of the forces acting horizontally on surface 201 is the sum of driving force 207 and the friction force developed at the interface of surface 201 and

- penetrating member 202, which acts in opposition to driving force 207. Since the coefficient of friction between surface 203 and penetrating member 202 is less than the coefficient of friction between surface 201 and penetrating member 202, penetrating member 202 and surface 201 will remain stationary with respect to each other and can be considered to behave as one piece when driving force 207 just exceeds the maximum frictional force that can be supported by the interface between surface 203 and penetrating member 202. Surface 201 and penetrating member 202 can be considered one piece because the coefficient of friction between surface 201 and penetrating member 202 is high enough to prevent relative motion between the two.
- 10 In one embodiment, the coefficient of friction between surface 201 and penetrating member 202 is approximately 0.8 corresponding to the coefficient of friction between two surfaces of stainless steel, while the coefficient of friction between surface 203 and penetrating member 202 is approximately 0.04, corresponding to the coefficient of friction between a surface of stainless steel and one of polytetrafluoroethylene.
- 15 Normal force 206 has a value of 202 Newtons. Using these values, the maximum frictional force that the interface between surface 201 and penetrating member 202 can support is 1.6 Newtons, while the maximum frictional force that the interface between surface 203 and penetrating member 202 can support is 0.08 Newtons. If driving force 207 exceeds 0.08 Newtons, surface 201 and penetrating member 202 will begin to accelerate together with respect to surface 203. Likewise, if driving force 207 exceeds 1.6 Newtons and penetrating member 202 encounters a rigid barrier, surface 201 would move relative to penetrating member 202.

Another condition, for example, for surface 201 to move relative to penetrating member 202 would be in the case of extreme acceleration. In an embodiment, penetrating member 202 has a mass of 8.24×10^{-6} kg. An acceleration of $194,174 \text{ m/s}^2$ of penetrating member 202 would therefore be required to exceed the frictional force between penetrating member 202 and surface 201, corresponding to approximately 19,800 g's. Without being bound to any particular embodiment or theory of operation, other methods of applying friction base coupling may also be used. For example, the penetrating member 202 may be engaged by a coupler using a interference fit to create the frictional engagement with the member.

Figure 14 illustrates a polytetrafluoroethylene coating on stainless steel surface 203 in detail. It should be understood that the surface 203 may be coated with other

materials such as but not limited to Telfon®, silicon, polymer or glass. The coating may cover all of the penetrating member, only the proximal portions, only the distal portions, only the tip, only some other portion, or some combination of some or all of the above.

Figure 15 illustrates a doping of lead applied to surface 201, which conforms to 5 penetrating member 202 microscopically when pressed against it. Both of these embodiments and other coated embodiments of a penetrating member may be used with the actuation methods described herein.

The shapes and configurations of surface 201 and surface 102 could be some form other than shown in Figures 12-15. For example, surface 201 could be the surface of a 10 wheel, which when rotated causes penetrating member 202 to advance or retract relative to surface 203. Surface 201 could be coated with another conformable material besides lead, such as but not limited to a plastic. It could also be coated with particles, such as but not limited to diamond dust, or given a surface texture to enhance the friction coefficient of surface 201 with penetrating member 202. Surface 202 could be made of or 15 coated with diamond, fluorinated ethylene propylene, perfluoroalkoxy, a copolymer of ethylene and tetrafluoroethylene, a copolymer of ethylene and chlorotrifluoroethylene, or any other material with a coefficient of friction with penetrating member 202 lower than that of the material used for surface 201.

Referring to Figure 16, a portion of a base plate 210 of an embodiment of a 20 penetrating member cartridge is shown with a plurality of penetrating member slots 212 disposed in a radial direction cut into a top surface 214 of the base plate. A drive member 216 is shown with a distal edge 218 disposed within one of the penetrating member slots 212 of the base plate 210. The distal edge 218 of the drive member 216 is configured to slide within the penetrating member slots 212 with a minimum of friction but with a close 25 fit to minimize lateral movement during a lancing cycle.

Figure 17 shows a distal portion 220 of a coated penetrating member 222 in partial longitudinal section. The coated penetrating member 222 has a core portion 224, a 30 coating 226 and a tapered distal end portion 228. A portion of a coated drive member 230 is shown having a coating 234 with penetrating member contact surface 236. The penetrating member contact surface 236 forms an interface 238 with an outer surface 240 of the coated penetrating member 222. The interface 238 has a characteristic friction coefficient that will depend in part on the choice of materials for the penetrating member coating 226 and the drive member coating 234. If silver is used as the penetrating

member and drive member coating 226 and 236, this yields a friction coefficient of about 1.3 to about 1.5. Other materials can be used for coatings 226 and 236 to achieve the desired friction coefficient. For example, gold, platinum, stainless steel and other materials may be used for coatings 226 and 236. It may be desirable to use combinations 5 of different materials for coatings 226 and 236. For example, an embodiment may include silver for a penetrating member coating 226 and gold for a drive member coating. Some embodiments of the interface 238 can have friction coefficients of about 1.15 to about 5.0, specifically, about 1.3 to about 2.0.

Embodiments of the penetrating member 222 can have an outer transverse 10 dimension or diameter of about 200 to about 400 microns, specifically, about 275 to about 325 microns. Embodiments of penetrating member 222 can have a length of about 10 to about 30 millimeters, specifically, about 15 to about 25 millimeters. Penetrating member 222 can be made from any suitable high strength alloy such as but not limited to stainless steel or the like.

15 Figure 18 is a perspective view of a lancing device 242 having features of the invention. A penetrating member cartridge 244 is disposed about a driver 246 that is coupled to a drive member 248 by a coupler rod 250. The penetrating member cartridge 244 has a plurality of penetrating member slots 252 disposed in a radial configuration in a top surface 254 a base plate 256 of the penetrating member cartridge 244. The distal ends 20 253 of the penetrating member slots 252 are disposed at an outer surface 260 of the base plate 256. A fracturable sterility barrier 258, shown partially cut away, is disposed on the top surface 254 of base plate 256 over the plurality of penetrating member slots 252. The sterility barrier 258 is also disposed over the outer surface 260 of the base plate 256 in order to seal the penetrating member slots from contamination prior to a lancing cycle. A 25 distal portion of a penetrating member 262 is shown extending radially from the penetrating member cartridge 244 in the direction of a patient's finger 264.

Figure 19 illustrates a portion of the base plate 256 used with the lancing device 242 in more detail and without sterility barrier 258 in place (for ease of illustration). The base plate 256 includes a plurality of penetrating member slots 252 which are in radial alignment with corresponding drive member slots 266. The drive member slots 266 have an optional tapered input configuration that may facilitate alignment of the drive member 30 248 during downward movement into the drive member slot 266 and penetrating member slot 252. Penetrating member slots 252 are sized and configured to accept a penetrating

member 262 disposed therein and allow axial movement of the penetrating member 262 within the penetrating member slots 252 without substantial lateral movement.

Referring again to Figure 18, in use, the present embodiment of penetrating member cartridge 242 is placed in an operational configuration with the driver 246. A lancing cycle is initiated and the drive member 248 is brought down through the sterility barrier 258 and into a penetrating member slot 252. A penetrating member contact surface of the drive member then makes contact with an outside surface of the penetrating member 262 and is driven distally toward the patient's finger 264 as described above with regard to the embodiment discussed in Figure 20. The friction coefficient between the penetrating member contact surface of the drive member 248 and the penetrating member 262 is greater than the friction coefficient between the penetrating member 262 and an interior surface of the penetrating member slots 252. As such, the drive member 248 is able to drive the penetrating member 262 distally through the sterility barrier 258 and into the patient's finger 264 without any relative movement or substantial relative movement between the drive member 248 and the penetrating member 262.

Referring to Figures 20-22, a lancing cycle sequence is shown for a lancing device 242 with another embodiment of a penetrating member cartridge 244 as shown in Figures 23 and 24. The base plate 256 of the penetrating member cartridge 242 shown in Figures 23 and 24 has a plurality of penetrating member slots 252 with top openings 268 that do not extend radially to the outer surface 260 of the base plate 256. In this way, the penetrating member slots 252 can be sealed with a first sterility barrier 270 disposed on the top surface 254 of the base plate 256 and a second sterility barrier 272 disposed on the outer surface 260 of the base plate 256. Penetrating member outlet ports 274 are disposed at the distal ends of the penetrating member slots 252.

Referring again to Figure 20, the penetrating member 262 is shown in the proximally retracted starting position within the penetrating member slot 252. The outer surface of the penetrating member 276 is in contact with the penetrating member contact surface 278 of the drive member 248. The friction coefficient between the penetrating member contact surface 278 of the drive member 248 and the outer surface 276 of the penetrating member 262 is greater than the friction coefficient between the penetrating member 262 and an interior surface 280 of the penetrating member slots 252. A distal drive force as indicated by arrow 282 in Figure 10 is then applied via the drive coupler 250 to the drive member 248 and the penetrating member is driven out of the penetrating

member outlet port 274 and into the patient's finger 264. A proximal retraction force, as indicated by arrow 284 in Figure 22, is then applied to the drive member 248 and the penetrating member 262 is withdrawn from the patient's finger 264 and back into the penetrating member slot 252.

- 5 Figures 25 and 26 illustrate an embodiment of a multiple layer sterility barrier 258 in the process of being penetrated by a penetrating member 62. It should be understood that this barrier 258 may be adapted for use with any embodiment of the present invention. The sterility barrier 258 shown in Figures 25 and 26 is a two layer sterility barrier 258 that facilitates maintaining sterility of the penetrating member 262 as it passes
- 10 through and exits the sterility barrier 258. In Figure 25, the distal end 286 of the penetrating member 262 is applying an axial force in a distal direction against an inside surface 288 of a first layer 290 of the sterility barrier 258, so as to deform the first layer 290 of the sterility barrier 258. The deformation 291 of the first layer 290 in turn applies a distorting force to the second layer 292 of the sterility barrier 258. The second layer of
- 15 the sterility barrier is configured to have a lower tensile strength than the first layer 290. As such, the second layer 292 fails prior to the first layer 290 due to the strain imposed on the first layer 290 by the distal end 286 of the penetrating member 262, as shown in Figure 26. After the second layer 292 fails, it then retracts from the deformed portion 291 of the first layer 290 as shown by arrows 294 in Figure 26. As long as the inside surface
- 20 288 and outside surface 296 of the first layer 290 are sterile prior to failure of the second layer 292, the penetrating member 262 will remain sterile as it passes through the first layer 290 once the first layer eventually fails. Such a multiple layer sterility barrier 258 can be used for any of the embodiments discussed herein. The multiple layer sterility barrier 258 can also include three or more layers.
- 25 Referring to Figures 27 and 28, an embodiment of a drive member 300 coupled to a driver 302 wherein the drive member 300 includes a cutting member 304 having a sharpened edge 306 which is configured to cut through a sterility barrier 258 of a penetrating member slot 252 during a lancing cycle in order for the drive member 300 to make contact with a penetrating member. An optional lock pin 308 on the cutting
- 30 member 304 can be configured to engage the top surface 310 of the base plate in order to prevent distal movement of the cutting member 304 with the drive member 300 during a lancing cycle.

Figures 29 and 30 illustrate an embodiment of a penetrating member slot 316 in longitudinal section having a ramped portion 318 disposed at a distal end 320 of the penetrating member slot. A drive member 322 is shown partially disposed within the penetrating member slot 316. The drive member 322 has a cutting edge 324 at a distal 5 end 326 thereof for cutting through a sterility barrier 328 during a lancing cycle. Figure 30 illustrates the cutting edge 324 cutting through the sterility barrier 328 during a lancing cycle with the cut sterility barrier 328 peeling away from the cutting edge 324.

Figures 31-34 illustrate drive member slots in a base plate 330 of a penetrating member cartridge wherein at least a portion of the drive member slots have a tapered 10 opening which is larger in transverse dimension at a top surface of the base plate than at the bottom of the drive member slot. Figure 31 illustrates a base plate 330 with a penetrating member slot 332 that is tapered at the input 334 at the top surface 336 of the base plate 330 along the entire length of the penetrating member slot 332. In such a configuration, the penetrating member slot and drive member slot (not shown) would be 15 in communication and continuous along the entire length of the slot 332. As an optional alternative, a base plate 338 as shown in Figure 32 and 33 can have a drive member slot 340 that is axially separated from the corresponding penetrating member slot 342. With this configuration, the drive member slot 340 can have a tapered configuration and the penetrating member slot 342 can have a straight walled configuration. In addition, this 20 configuration can be used for corrugated embodiments of base plates 346 as shown in Figure 34. In Figure 34, a drive member 348 is disposed within a drive member slot 350. A penetrating member contact surface 352 is disposed on the drive member 348. The contact surface 352 has a tapered configuration that will facilitate lateral alignment of the drive member 348 with the drive member slot 350.

Figures 35-37 illustrate an embodiment of a penetrating member cartridge 360 and drive member 362 wherein the drive member 362 has contoured jaws 364 configured to grip a penetrating member shaft 366. In Figure 35, the drive member 362 and penetrating member shaft 366 are shown in transverse cross section with the contoured jaws 364 disposed about the penetrating member shaft 366. A pivot point 368 is disposed between 25 the contoured jaws 364 and a tapered compression slot 370 in the drive member 362. A compression wedge 372 is shown disposed within the tapered compression slot 370. Insertion of the compression wedge 372 into the compression slot 370 as indicated by

arrow 374, forces the contoured jaws 364 to close about and grip the penetrating member shaft 366 as indicated by arrows 376.

Figure 36 shows the drive member 362 in position about a penetrating member shaft 366 in a penetrating member slot 378 in the penetrating member cartridge 360. The 5 drive member can be actuated by the methods discussed above with regard to other drive member and driver embodiments. Figure 37 is an elevational view in longitudinal section of the penetrating member shaft 166 disposed within the penetrating member slot 378. The arrows 380 and 382 indicate in a general way, the path followed by the drive member 362 during a lancing cycle. During a lancing cycle, the drive member comes down into 10 the penetrating member slot 378 as indicated by arrow 380 through an optional sterility barrier (not shown). The contoured jaws of the drive member then clamp about the penetrating member shaft 366 and move forward in a distal direction so as to drive the penetrating member into the skin of a patient as indicated by arrow 382.

Figures 38 and 39 show a portion of a lancing device 390 having a lid 392 that can 15 be opened to expose a penetrating member cartridge cavity 394 for removal of a used penetrating member cartridge 396 and insertion of a new penetrating member cartridge 398. Depression of button 400 in the direction indicated by arrow 402 raises the drive member 404 from the surface of the penetrating member cartridge 396 by virtue of lever action about pivot point 406. Raising the lid 392 actuates the lever arm 408 in the 20 direction indicated by arrow 410 which in turn applies a tensile force to cable 412 in the direction indicated by arrow 414. This action pulls the drive member back away from the penetrating member cartridge 396 so that the penetrating member cartridge 396 can be removed from the lancing device 390. A new penetrating member cartridge 398 can then be inserted into the lancing device 390 and the steps above reversed in order to position 25 the drive member 404 above the penetrating member cartridge 398 in an operational position.

Figures 40 and 41 illustrate a penetrating member cartridge 420 that has 30 penetrating member slots 422 on a top side 424 and a bottom side 426 of the penetrating member cartridge 420. This allows for a penetrating member cartridge 420 of a diameter D to store for use twice the number of penetrating members as a one sided penetrating member cartridge of the same diameter D.

Figures 42-44 illustrate end and perspective views of a penetrating member cartridge 430 having a plurality of penetrating member slots 432 formed from a

corrugated surface 434 of the penetrating member cartridge 430. Penetrating members 436 are disposed on both sides of the penetrating member cartridge 430. A sterility barrier 438 is shown disposed over the penetrating member slots 432 in Figure 44.

- Figures 45-48 illustrate embodiments of a penetrating member 440 and drive member 442 wherein the penetrating member 440 has a transverse slot 444 in the penetrating member shaft 446 and the drive member 442 has a protuberance 448 configured to mate with the transverse slot 444 in the penetrating member shaft 446. Figure 45 shows a protuberance 448 having a tapered configuration that matches a tapered configuration of the transverse slot 444 in the penetrating member shaft 446.
- 10 Figure 46 illustrates an optional alternative embodiment wherein the protuberance 448 has straight walled sides that are configured to match the straight walled sides of the transverse slot 444 shown in Figure 46. Figure 47 shows a tapered protuberance 448 that is configured to leave an end gap 450 between an end of the protuberance 448 and a bottom of the transverse slot in the penetrating member shaft 446.
- 15 Figure 48 illustrates a mechanism 452 to lock the drive member 442 to the penetrating member shaft 446 that has a lever arm 454 with an optional bearing 456 on the first end 458 thereof disposed within a guide slot 459 of the drive member 442. The lever arm 454 has a pivot point 460 disposed between the first end 458 of the lever arm 454 and the second end 462 of the lever arm 454. A biasing force is disposed on the
- 20 second end 462 of the lever arm 454 by a spring member 464 that is disposed between the second end 462 of the lever arm 454 and a base plate 466. The biasing force in the direction indicated by arrow 468 forces the penetrating member contact surface 470 of the drive member 442 against the outside surface of the penetrating member 446 and, in addition, forces the protuberance 448 of the drive member 442 into the transverse slot 444 of the penetrating member shaft 446.
- 25

Referring now to Figure 49, another embodiment of a replaceable cartridge 500 suitable for housing a plurality of individually moveable penetrating members (not shown) will be described in further detail. Although cartridge 500 is shown with a chamfered outer periphery, it should also be understood that less chamfered and unchamfered embodiments of the cartridge 500 may also be adapted for use with any embodiment of the present invention disclosed herein. The penetrating members slidably coupled to the cartridge may be a bare lancet or bare elongate member without outer molded part or body pieces as seen in conventional lancet. The bare design reduces cost

and simplifies manufacturing of penetrating members for use with the present invention. The penetrating members may be retractable and held within the cartridge so that they are not able to be used again. The cartridge is replaceable with a new cartridge once all the piercing members have been used. The lancets or penetrating members may be fully contained in the used cartridge so as to minimize the chance of patient contact with such waste.

As can be seen in Figure 49, the cartridge 500 may include a plurality of cavities 501 for housing a penetrating member. In this embodiment, the cavity 501 may have a longitudinal opening 502 associated with the cavity. The cavity 501 may also have a lateral opening 503 allowing the penetrating member to exit radially outward from the cartridge. As seen in Figure 49, the outer radial portion of the cavity may be narrowed. The upper portion of this narrowed area may also be sealed or swaged to close the top portion 505 and define an enclosed opening 506 as shown in Figure 50. Optionally, the narrowed area 504 may retain an open top configuration, though in some embodiments, the foil over the gap is unbroken, preventing the penetrating member from lifting up or extending upward out of the cartridge. The narrowed portion 504 may act as a bearing and/or guide for the penetrating member. Figure 51 shows that the opening 506 may have a variety of shapes such as but not limited to, circular, rectangular, triangular, hexagonal, square, or combinations of any or all of the previous shapes. Openings 507 (shown in phantom) for other microfluidics, capillary tubes, or the like may also be incorporated in the immediate vicinity of the opening 506. In some optional embodiments, such openings 507 may be configured to surround the opening 506 in a concentric or other manner.

Referring now to Figure 52, the underside of a cartridge 500 will be described in further detail. This figure shows many features on one cartridge 500. It should be understood that a cartridge may include some, none, or all of these features, but they are shown in Figure 52 for ease of illustration. The underside may include indentations or holes 510 close to the inner periphery for purpose of properly positioning the cartridge to engage a penetrating member gripper and/or to allow an advancing device (shown in Figure 56B and 56C) to rotate the cartridge 500. Indentations or holes 511 may be formed along various locations on the underside of cartridge 500 and may assume various shapes such as but not limited to, circular, rectangular, triangular, hexagonal, square, or combinations of any or all of the previous shapes. Notches 512 may also be formed along the inner surface of the cartridge 500 to assist in alignment and/or rotation of the

cartridge. It should be understood of course that some of these features may also be placed on the topside of the cartridge in areas not occupied by cavities 501 that house the penetrating members. Notches 513 may also be incorporated along the outer periphery of the cartridge. These notches 513 may be used to gather excess material from the sterility barrier 28 (not shown) that may be used to cover the angled portion 514 of the cartridge. In the present embodiment, the cartridge has a flat top surface and an angled surface around the outside. Welding a foil type sterility barrier over that angled surface, the foil folds because of the change in the surfaces which is now at 45 degrees. This creates excess material. The grooves or notches 513 are there as a location for that excess material. Placing the foil down into those grooves 513 which may tightly stretch the material across the 45 degree angled surface. Although in this embodiment the surface is shown to be at 45 degrees, it should be understood that other angles may also be used. For example, the surface may be at any angle between about 3 degrees to 90 degrees, relative to horizontal. In some embodiments, the surface may be squared off. The surface may be unchamfered. The surface may also be a curved surface or it may be combinations of a variety of angled surfaces, curved and straight surfaces, or any combination of some or all of the above.

Referring now to Figures 53-54, the sequence in which the cartridge 500 is indexed and penetrating members are actuated will now be described. It should be understood that some steps described herein may be combined or taken out of order without departing from the spirit of the invention. These sequence of steps provides vertical and horizontal movement used with the present embodiment to load a penetrating member onto the driver.

As previously discussed, each cavity on the cartridge may be individually sealed with a foil cover or other sterile enclosure material to maintain sterility until or just before the time of use. In the present embodiment, penetrating members are released from their sterile environments just prior to actuation and are loaded onto a launcher mechanism for use. Releasing the penetrating member from the sterile environment prior to launch allows the penetrating member in the present embodiment to be actuated without having to pierce any sterile enclosure material which may dull the tip of the penetrating member or place contaminants on the member as it travels towards a target tissue. A variety of methods may be used accomplish this goal.

Figure 53A shows one embodiment of penetrating member release device, which in this embodiment is a punch plate 520 that is shown in a see-through depiction for ease of illustration. The punch plate 520 may include a first portion 521 for piercing sterile material covering the longitudinal opening 502 and a second portion 522 for piercing material covering the lateral opening 503. A slot 523 allows the penetrating member gripper to pass through the punch plate 520 and engage a penetrating member housed in the cartridge 500. The second portion 522 of the punch plate down to engage sterility barrier angled at about a 45 degree slope. Of course, the slope of the barrier may be varied. The punch portion 521 first contacts the rear of the front pocket sterility barrier and as it goes down, the cracks runs down each side and the barrier is pressed down to the bottom of the front cavity. The rear edge of the barrier first contacted by the punch portion 522 is broken off and the barrier is pressed down, substantially cleared out of the way. These features may be more clearly seen in Figure 53B. The punch portion 521 may include a blade portion down the centerline. As the punch comes down, that blade may be aligned with the center of the cavity, cutting the sterility barrier into two pieces. The wider part of the punch 521 then pushes down on the barrier so the they align parallel to the sides of the cavity. This creates a complete and clear path for the gripper throughout the longitudinal opening of the cavity. Additionally, as seen in Figure 53B and 54A, a plurality of protrusion 524 are positioned to engage a cam (Figure 55A) which sequences the punching and other vertical movement of punch plate 520 and cartridge pusher 525. The drive shaft 526 from a force generator (not shown) which is used to actuate the penetrating member 527.

Referring now to Figures 54A-F, the release and loading of the penetrating members are achieved in the following sequence. Figure 54A shows the release and loading mechanism in rest state with a dirty bare penetrating member 527 held in a penetrating member gripper 530. This is the condition of the device between lancing events. When the time comes for the patient to initiate another lancing event, the used penetrating member is cleared and a new penetrating member is loaded, just prior to the actual lancing event. The patient begins the loading of a new penetrating member by operating a setting lever or slider to initiate the process. The setting lever may operate mechanically to rotate a cam (see Figure 55A) that moves the punch plate 520 and cartridge pusher 525. A variety of mechanisms can be used to link the slider to cause rotation of the cartridge. In other embodiments, a stepper motor or other mover such as

but not limited to, a pneumatic actuator, hydraulic actuator, or the like are used to drive the loading sequence.

Figure 54B shows one embodiment of penetrating member gripper 530 in more detail. The penetrating member gripper 530 may be in the form of a tuning fork with sharp edges along the inside of the legs contacting the penetrating member. In some embodiments, the penetrating member may be notched, recessed, or otherwise shaped to receive the penetrating member gripper. As the gripper 530 is pushed down on the penetrating member, the legs are spread open elastically to create a frictional grip with the penetrating member such as but not limited to bare elongate wires without attachments molded or otherwise attached thereon. In some embodiments, the penetrating member is made of a homogenous material without any additional attachments that are molded, adhered, glued or otherwise added onto the penetrating member.

In some embodiments, the gripper 530 may cut into the sides of the penetrating member. The penetrating member in one embodiment may be about 300 microns wide. The grooves that form in the side of the penetrating member by the knife edges are on the order of about 5-10 microns deep and are quite small. In this particular embodiment, the knife edges allow the apparatus to use a small insertion force to get the gripper onto the penetrating member, compared to the force to remove the penetrating member from the gripper the longitudinal axis of an elongate penetrating member. Thus, the risk of a penetrating member being detached during actuation are reduced. The gripper 530 may be made of a variety of materials such as, but not limited to high strength carbon steel that is heat treated to increased hardness, ceramic, substrates with diamond coating, composite reinforced plastic, elastomer, polymer, and sintered metals. Additionally, the steel may be surface treated. The gripper 130 may have high gripping force with low friction drag on solenoid or other driver.

As seen in Figure 54C, the sequence begins with punch plate 520 being pushed down. This results in the opening of the next sterile cavity 532. In some embodiment, this movement of punch plate 520 may also result in the crimping of the dirty penetrating member to prevent it from being used again. This crimping may result from a protrusion on the punch plate bending the penetrating member or pushing the penetrating member into a groove in the cartridge that hold the penetrating member in place through an interference fit. As seen in Figures 53B and 54C, the punch plate 520 has a protrusion or punch shaped to penetrate a longitudinal opening 502 and a lateral opening 503 on the

cartridge. The first portion 521 of the punch that opens cavity 532 is shaped to first pierce the sterility barrier and then push, compresses, or otherwise moves sterile enclosure material towards the sides of the longitudinal opening 502. The second portion 522 of the punch pushes down the sterility barrier at lateral opening or penetrating member exit 503 such that the penetrating member does not pierce any materials when it is actuated toward a tissue site.

Referring now to Figure 54D, the cartridge pusher 525 is engaged by the cam 550 (not shown) and begins to push down on the cartridge 500. The punch plate 520 may also travel downward with the cartridge 500 until it is pushed down to its maximum downward position, while the penetrating member gripper 530 remains vertically stationary. This joint downward motion away from the penetrating member gripper 530 will remove the penetrating member from the gripper. The punch plate 520 essentially pushes against the penetrating member with protrusion 534 (Figure 55A), holding the penetrating member with the cartridge, while the cartridge 500 and the punch plate 520 is lowered away from the penetrating member gripper 530 which in this embodiment remains vertically stationary. This causes the stripping of the used penetrating member from the gripper 530 (Figure 45D) as the cartridge moves relative to the gripper.

At this point as seen in Figure 54E, the punch plate 520 retracts upward and the cartridge 500 is pushed fully down, clear of the gripper 530. Now cleared of obstructions and in a rotatable position, the cartridge 500 increments one pocket or cavity in the direction that brings the newly released, sterile penetrating member in cavity 532 into alignment with the penetrating member gripper 530, as seen in Figure 54F. The rotation of the cartridge occurs due to fingers engaging the holes or indentations 533 on the cartridge, as seen in Figure 54A. In some embodiments, these indentations 533 do not pass completely through cartridge 500. In other embodiments, these indentations are holes passing completely through. The cartridge has a plurality of little indentations 533 on the top surface near the center of the cartridge, along the inside diameter. In the one embodiment, the sterility barrier is cut short so as not to cover these plurality of indentations 533. It should be understood of course that these holes may be located on bottom, side or other accessible surface. These indentations 533 have two purposes. The apparatus may have one or a plurality of locator pins, static pins, or other keying feature that does not move. In this embodiment, the cartridge will only set down into positions where the gripper 530 is gripping the penetrating member. To index the cassette, the

cartridge is lifted off those pins or other keyed feature, rotated around, and dropped onto those pins for the next position. The rotating device is through the use of two fingers: one is a static pawl and the other one is a sliding finger. They engage with the holes 533. The fingers are driven by a slider that may be automatically actuated or actuated by the user.

- 5 This maybe occur mechanically or through electric or other powered devices. Halfway through the stroke, a finger may engage and rotate around the cartridge. A more complete description can be found with text associated with Figures 56B-56C.

Referring now to Figure 54G, with the sterile penetrating member in alignment, the cartridge 500 is released as indicated by arrows 540 and brought back into contact 10 with the penetrating member gripper 530. The new penetrating member 541 is inserted into the gripper 530, and the apparatus is ready to fire once again. After launch and in between lancing events for the present embodiment, the bare lancet or penetrating member 541 is held in place by gripper 530, preventing the penetrating member from accidentally protruding or sliding out of the cartridge 500.

15 It should be understood of course, that variations can be added to the above embodiment without departing from the spirit of the invention. For example, the penetrating member 541 may be placed in a parked position in the cartridge 500 prior to launch. As seen in Figure 55A, the penetrating member may be held by a narrowed portion 542 of the cartridge, creating an interference fit which pinches the proximal end 20 of the penetrating member. Friction from the molding or cartridge holds the penetrating member during rest, preventing the penetrating member from sliding back and forth. Of course, other methods of holding the penetrating member may also be used. As seen in Figure 55B prior to launch, the penetrating member gripper 530 may pull the penetrating member 541 out of the portion 542. The penetrating member 541 may remain in this 25 portion until actuated by the solenoid or other force generator coupled to the penetrating member gripper. A cam surface 544 may be used to pull the penetrating member out of the portion 542. This mechanical cam surface may be coupled to the mechanical slider driven by the patient, which may be considered a separate force generator. Thus, energy from the patient extracts the penetrating member and this reduces the drain on the 30 device's battery if the solenoid or electric driver were to pull out the penetrating member. The penetrating member may be moved forward a small distance (on the order of about 1 mm or less) from its parked position to pull the penetrating member from the rest position gripper. After penetrating tissue, the penetrating member may be returned to the cartridge

and eventually placed into the parked position. This may also occur, though not necessarily, through force provided by the patient. In one embodiment, the placing of the lancet into the parked position does not occur until the process for loading a new penetrating member is initiated by the patient. In other embodiments, the pulling out of the parked position occurs in the same motion as the penetrating member actuation. The return into the parked position may also be considered a continuous motion.

Figure 55A also shows one embodiment of the cam and other surfaces used to coordinate the motion of the punch plate 520. For example, cam 550 in this embodiment is circular and engages the protrusions 524 on the punch plate 520 and the cartridge pusher 525. Figure 55A also more clearly shows protrusion 534 which helps to hold the penetrating member in the cartridge 500 while the penetrating member gripper 530 pulls away from the member, relatively speaking. A ratchet surface 552 that rotates with the cam 550 may be used to prevent the cam from rotating backwards. The raising and lowering of cartridge 500 and punch plate 50 used to load/unload penetrating members may be mechanically actuated by a variety of cam surfaces, springs, or the like as may be determined by one skilled in the art. Some embodiments may also use electrical or magnetic device to perform the loading, unloading, and release of bare penetrating members. Although the punch plate 520 is shown to be punching downward to displace, remove, or move the foil or other sterile environment enclosure, it should be understood that other methods such as but not limited to stripping, pulling, tearing, or some combination of one or more of these methods may be used to remove the foil or sterile enclosure. For example, in other embodiments, the punch plate 520 may be located on an underside of the cartridge and punch upward. In other embodiments, the cartridge may remain vertically stationary while other parts such as but not limited to the penetrating member gripper and punch plate move to load a sterile penetrating member on to the penetrating member gripper.

Figure 55B also shows other features that may be included in the present apparatus. A fire button 560 may be included for the user to actuate the penetrating member. A front end interface 561 may be included to allow a patient to seat their finger or other target tissue for lancing. The interface 561 may be removable to be cleaned or replaced. A visual display 562 may be included to show device status, lancing performance, error reports, or the like to the patient.

- Referring now to Figure 56A, a mechanical slider 564 used by the patient to load new penetrating member may also be incorporated on the housing. The slider 564 may also be coupled to activate an LCD or visual display on the lancing apparatus. In addition to providing a source of energy to index the cartridge, the slider 564 may also switch the electronics to start the display. The user may use the display to select the depth of lancing or other feature. The display may go back to sleep again until it is activated again by motion of the slider 564. The underside the housing 566 may also be hinged or otherwise removable to allow the insertion of cartridge 500 into the device. The cartridge 500 may be inserted using technology current used for insertion of a compact disc or other disc
- 5 into a compact disc player. In one embodiment, there may be a tray which is deployed outward to receive or to remove a cartridge. The tray may be withdrawn into the apparatus where it may be elevated, lowered, or otherwise transported into position for use with the penetrating member driver. In other embodiments, the apparatus may have a slot into which the cartridge is partially inserted at which point a mechanical apparatus
- 10 will assist in completing insertion of the cartridge and load the cartridge into proper position inside the apparatus. Such device is akin to the type of compact disc player found on automobiles. The insertions/ejection and loading apparatus of these compact disc players uses gears, pulleys, cables, trays, and/or other parts that may be adapted for use with the present invention.
- 15 Referring now to Figure 56B, a more detailed view of one embodiment of the slider 564 is provided. In this embodiment, the slider 564 will move initially as indicated by arrow 567. To complete the cycle, the patient will return the slider to its home position or original starting position as indicated by arrow 568. The slider 564 has an arm 569 which moves with the slider to rotate the cam 550 and engage portions 522. The motion of the slider 564 is also mechanically coupled to a finger 570 which engage the indentations 571 on cartridge 500. The finger 570 is synchronized to rotate the cartridge 500 by pulling as indicated by arrow 572 in the same plane as the cartridge. It should be understood that in some embodiments, the finger 570 pushes instead of pulls to rotate the cartridge in the correct direction. The finger 570 may also be adapted to engage ratchet
- 20 surfaces 706 as seen in Figure 66 to rotate a cartridge. The finger 570 may also incorporate vertical motion to coordinate with the rising and lowering of the cartridge 500. The motion of finger 570 may also be powered by electric actuators such as but not

limited to a stepper motor or other device useful for achieving motion. Figure 56B also shows a portion of the encoder 573 used in position sensing.

Referring now to Figure 56C, a still further view of the slider 564 and arm 569 is shown. The arm 569 moves to engage portion 522 as indicated by arrow 575 and this causes the cam 550 to rotate as indicated by arrow 577. In this particular embodiment, the cam 550 rotates about 1/8 of an rotation with each pull of the slider 564. When the slider 564 is return to its home or start position, the arm 569 rides over the portion 522. The movement of the slider also allows the cam surface 544 to rotate about pivot point 579. A resilient member 580 may be coupled to the cam surface 544 to cause it to rotate counterclockwise when the arm 569 moves in the direction of arrow 567. The pin 580 will remain in contact with the arm 569. As the cam surface 544 rotates a first surface 582 will contact the pin 583 on the gripper block 584 and pull the pin 583 back to park a penetrating member into a coupling or narrowed portion 542 of the cartridge 500 as seen in Figure 55A. As the arm 569 is brought back to the home position, the cam surface 544 rotates back and a second surface 586 that rotates clockwise and pushes the penetrating member forward to be released from the narrowed portion 542 resulting in a position as seen in Figure 55B. It should be understood that in some embodiments, the release and/or parking of lancet from portion 542 may be powered by the driver 588 without using the mechanical assistance from cam surface 544.

In another embodiment of the cartridge device, a mechanical feature may be included on the cartridge so that there is only one way to load it into the apparatus. As a nonlimiting example, in one embodiment holding 50 penetrating members, the cartridge may have 51 pockets or cavities. The 51st pocket will go into the firing position when the device is loaded, thus providing a location for the gripper to rest in the cartridge without releasing a penetrating member from a sterile environment. The gripper 530 in that zeroth position is inside the pocket or cavity and that is the reason why one of the pockets may be empty. Of course, some embodiments may have the gripper 530 positioned to grip a penetrating member as the cartridge 500 is loaded into the device, with the patient lancing themselves soon afterwards so that the penetrating member is not contaminated due to prolonged exposure outside the sterile enclosure. That zeroth position may be the start and finish position. The cartridge may also be notched to engaged a protrusion on the apparatus, thus also providing a method for allowing the penetrating member to loaded or unloaded only in one orientation. Essentially, the cartridge 500 may be keyed

or slotted in association with the apparatus so that the cartridge 500 can only be inserted or removed at one orientation. For example as seen in Figure 56D, the cartridge 592 may have a keyed slot 593 that matches the outline of a protrusion 594 such that the cartridge 592 may only be removed upon alignment of the slot 593 and protrusion 594 upon at the 5 start or end positions. It should be understood that other keyed technology may be used and the slot or key may be located on an outer periphery or other location on the cartridge 592 in manner useful for allowing insertion or removal of the cartridge from only one or a select number of orientations.

Referring now to Figure 57, a cross-section of another embodiment of a cavity 10 600 housing a penetrating member is shown. The cavity 600 may include a depression 602 for allowing the gripper 530 to penetrate sufficiently deeply into the cavity to frictionally engage the penetrating member 541. The penetrating member may also be housed in a groove 604 that holds the penetrating member in place prior to and after actuation. The penetrating member 541 is lifted upward to clear the groove 604 during 15 actuation and exits through opening 506.

Referring now to Figure 58, another variation on the system according to the present invention will now be described. Figure 58 shows a lancing system 610 wherein the penetrating members have their sharpened tip pointed radially inward. The finger or other tissue of the patient is inserted through the center hole 611 to be pierced by the 20 member 612. The penetrating member gripper 530 coupled to drive force generator 613 operate in substantially the same manner as described in Figures 54A-G. The punch portions 521 and 522 operate in substantially the same manner to release the penetrating members from the sterile enclosures. The punch portion 522 may be placed on the inner periphery of the device, where the penetrating member exit is now located, so that sterile 25 enclosure material is cleared out of the path of the penetrating member exit.

Referring now to Figure 59, a still further variation on the lancing system according to the present invention will now be described. In the embodiments shown in Figures 53-54, the penetrating member gripper 530 approaches the penetrating member from above and at least a portion of the drive system is located in a different plane from 30 that of the cartridge 500. Figure 59 shows an embodiment where the penetrating member driver 620 is in substantially the same plane as the penetrating member 622. The coupler 624 engages a bent or L shaped portion 626 of the member 622. The cartridge 628 can rotate to engage a new penetrating member with the coupler 624 without having to move

the cartridge or coupler vertically. The next penetrating member rotates into position in the slot provided by the coupler 624. A narrowed portion of the cartridge acts as a penetrating member guide 630 near the distal end of the penetrating member to align the penetrating member as it exits the cartridge.

5 The coupler 624 may come in a variety of configurations. For example, Figure 60A shows a coupler 632 which can engage a penetrating member 633 that does not have a bent or L-shaped portion. A radial cartridge carrying such a penetrating member 633 may rotate to slide penetrating member into the groove 634 of the coupler 632. Figure 60B is a front view showing that the coupler 632 may include a tapered portion 636 to 10 guide the penetrating member 633 into the slot 634. Figure 60C shows an embodiment of the driver 620 using a coupler 637 having a slot 638 for receiving a T-shaped penetrating member. The coupler 637 may further include a protrusion 639 that may be guided in an overhead slot to maintain alignment of the drive shaft during actuation.

15 Referring now to Figure 61, a cartridge 640 for use with an in-plane driver 620 is shown. The cartridge 640 includes an empty slot 642 that allows the cartridge to be placed in position with the driver 620. In this embodiment, the empty slot 642 allows the coupler 644 to be positioned to engage an unused penetrating member 645 that may be rotated into position as shown by arrow 646. As seen in Figure 61, the cartridge 640 may also be designed so that only the portion of the penetrating member that needs to remain 20 sterile (i.e. the portions that may actually be penetrating into tissue) are enclosed. As seen in Figure 61, a proximal portion 647 of the penetrating member is exposed. This exposed proximal portion may be about 70% of the penetrating member. In other embodiments it may be between about 69% to about 5% of the penetrating member. The cartridge 640 may further include, but not necessarily, sealing protrusions 648. These protrusions 648 25 are releasably coupled to the cartridge 640 and are removed from the cartridge 640 by remover 649 as the cartridge rotates to place penetrating member 645 into the position of the active penetrating member. The sterile environment is broken prior to actuation of the member 645 and the member does not penetrate sterile enclosure material that may dull the tip of the penetrating member during actuation. A fracturable seal material 650 may 30 be applied to the member to seal against an inner peripheral portion of the cartridge.

Referring now to Figure 62, a still further embodiment of a cartridge for use with the present invention will be described. This cartridge 652 includes a tapered portion 654 for allowing the coupler 655 to enter the cavity 656. A narrowed portion 657 guides the

penetrating member 658. The coupler 655 may have, but does not necessarily have, movable jaws 659 that engage to grip the penetrating member 658. Allowing the coupler to enter the cavity 656 allows the alignment of the penetrating member to be better maintained during actuation. This tapered portion 654 may be adapted for use with any 5 embodiment of the cartridge disclosed herein.

Referring now to Figure 63, a linear cartridge 660 for use with the present invention will be described. Although the present invention has been shown in use with radial cartridges, the lancing system may be adapted for use with cartridges of other shapes. Figures 79-83 show other cartridges of varying shapes adaptable for use with the 10 present invention. Figure 63 illustrates a cartridge 660 with only a portion 662 providing sterile protection for the penetrating members. The cartridge 660, however, provides a base 664 on which a penetrating member 665 can rest. This provides a level of protection of the penetrating member during handling. The base 664 may also be shaped to provide slots 666 in which a penetrating member 667 may be held. The slot 666 may also be 15 adapted to have a tapered portion 668. These configurations may be adapted for use with any of the embodiments disclosed herein, such as the cartridge 652.

Referring now to Figures 64A-64C, a variety of different devices are shown for releasing the sterility seal covering a lateral opening 503 on the cartridge 500. Figure 64A shows a rotating punch device 670 that has protrusions 672 that punch out the 20 sterility barrier creating openings 674 from which a penetrating member can exit without touching the sterility barrier material. Figure 64B shows a vertically rotating device 676 with shaped protrusions 678 that punch down the sterility barrier 679 as it is rotated to be in the active, firing position. Figure 64C shows a punch 680 which is positioned to punch out barrier 682 when the cartridge is lowered onto the punch. The cartridge is rotated and 25 the punch 680 rotates with the cartridge. After the cartridge is rotated to the proper position and lifted up, the punch 680 is spring loaded or otherwise configured to return to the position to engage the sterility barrier covering the next unused penetrating member.

Referring now to Figure 65A-65B, another type of punch mechanism for use with a punch plate 520 will now be described. The device shown in Figures 53-54 shows a 30 mechanism that first punches and then rotates or indexes the released penetrating member into position. In this present embodiment, the cartridge is rotated first and then the gripper and punch may move down simultaneously. Figure 65A shows one embodiment of a punch 685 having a first portion 686 and a second portion 687. As seen in cross-

sectional view of Figure 65B, the penetrating member gripper 690 is located inside the punch 685. Thus the penetrating of the sterility barrier is integrated into the step of engaging the penetrating member with the gripper 690. The punch 685 may include a slot 692 allowing a portion 694 of the gripper 690 to extend upward. A lateral opening 695 is 5 provided from which a penetrating member may exit. In some embodiments, the punch portion 687 is not included with punch 686; instead relying on some other mechanism such as those shown in Figures 64A-64C to press down on barrier material covering a lateral opening 503.

Referring now to Figures 66, a still further embodiment of a cartridge according to 10 the present invention will be described. Figure 66 shows a cartridge 700 with a plurality of cavities 702 and individual deflectable portions or fingers 704. The ends of the protective cavities 702 may be divided into individual fingers (such as one for each cavity) on the outer periphery of the disc. Each finger 704 may be individually sealed with a foil cover (not shown for ease of illustration) to maintain sterility until the time of 15 use. Along the inner periphery of the cartridge 700 are raised step portions 706 to create a ratchet type mechanism. As seen in Figure 67, a penetrating member 708 may be housed in each cavity. The penetrating member may rest on a raised portion 710. A narrowed portion 712 pinches the proximal portions of the penetration member 708. Each cavity may include a wall portion 714 into which the penetrating member 708 may 20 be driven after the penetrating member has been used. Figure 68 shows the penetrating member gripper 716 lowered to engage a penetrating member 708. For ease of illustration, a sterility barrier covering each of the cavities is not shown.

Referring now to Figures 69A-69L, the sequence of steps for actuating a 25 penetrating member in a cartridge 700 will be described. It should be understood that in other embodiments, steps may be combined or reduced without departing from the spirit of the present invention. The last penetrating member to be used may be left in a retracted position, captured by a gripper 716. The end of the protective cavity 704 may be deflected downward by the previous actuation. The user may operate a mechanism such as but not limited to a thumbwheel, lever, crank, slider, etc...that advances a new 30 penetrating member 720 into launch position as seen in Figure 69A. The mechanism lifts a bar that allows the protective cavity to return to its original position in the plane of the disc.

In this embodiment as shown in Figure 69B, the penetrating member guide 722 presses through foil in rear of pocket to "home" penetrating member and control vertical clearance. For ease of illustration, actuation devices for moving the penetrating member guide 722 and other mechanisms are not shown. They may be springs, cams, or other devices that can lower and move the components shown in these figures. In some embodiments, the cartridge 700 may be raised or lowered to engage the penetrating member guide 722 and other devices.

As seen in Figure 69C, the plough or sterile enclosure release device 724 is lowered to engage the cartridge 700. In some embodiments, the disc or cartridge 700 may be raised part way upward until a plough or plow blade 724 pierces the sterility barrier 726 which may be a foil covering.

Referring now to Figure 69D, the plough 724 clears foil from front of pocket and leaves it attached to cartridge 700. The plough 724 is driven radially inward, cutting open the sterility barrier and rolling the scrap into a coil ahead of the plough. Foil naturally curls over and forms tight coil when plough lead angle is around 55deg to horizontal. If angle of the plough may be between about 60-40deg, preferably closer to 55 degs. In some embodiments, the foil may be removed in such a manner that the penetrating member does not need to pierce any sterile enclosure materials during launch.

Referring now to Figure 69E, the gripper 716 may be lowered to engage the bare penetrating member or piercing member 720. Optionally, the disc or cartridge 8000 may be raised until the penetrating member 720 is pressed firmly into the gripper 716.

Although not shown in the present figure, the penetrating member driver or actuator of the present embodiment may remain in the same horizontal plane as the penetrating member.

As seen in Figure 69F, a bar 730 may be pressed downward on the outer end 732 of the protective cavity to deflect it so it is clear of the path of the penetrating member. In the present embodiment, the bar 730 is shaped to allow the bare penetrating member 720 to pass through. It should be understood that other shapes and orientations of the bar (such as contacting only one side or part of end 732) may be used to engage the end 732.

Referring now to Figure 69G, an electrical solenoid or other electronic or feed-back controllable drive may actuate the gripper 716 radially outward, carrying the bare penetrating member 720 with it. The bare penetrating member projects from the protective case and into the skin of a finger or other tissue site that has been placed over

the aperture of the actuator assembly. Suitable penetrating member drivers are described in commonly assigned, copending U.S. Patent Application Ser. No. 10/127,395 (Attorney Docket No. 38187-2551) filed April 19, 2002.

Referring now to Figure 69H, the solenoid or other suitable penetrating member driver retracts the bare penetrating member 720 into a retracted position where it parks until the beginning of the next lancing cycle.

Referring now to Figure 69I, bar 730 may be released so that the end 150 returns to an in-plane configuration with the cartridge 800.

As seen in Figure 69J, the gripper 716 may drive a used bare penetrating member 10 radially outward until the sharpened tip is embedded into a plastic wall 714 at or near the outward end 732 of the cavity thus immobilizing the contaminated penetrating member.

As seen in Figures 69K and 69L, the plough 724, the gripper 716, and penetrating member guide 722 may all be disengaged from the bare penetrating member 720.

Optionally, it should be understood that the advance mechanism may lower the cartridge 15 700 from the gripper 716. The used penetrating member, restrained by the tip embedded in plastic, and by the cover foil at the opposite end, is stripped from the gripper. The disc or cartridge 700 may be rotated until a new, sealed; sterile penetrating member is in position under the launch mechanism.

- Referring now to Figures 70 and 71, one object for some embodiments of the invention is to include blood sampling and sensing on this penetrating member actuation device. In the present embodiment, the drive mechanism (gripper 738 and solenoid drive coil 739) may be used to drive a penetrating member into the skin and couple this lancing event to acquire the blood sample as it forms at the surface of the finger. In a first embodiment shown in Figure 70, microfluidic module 740 bearing the analyte detecting member chemistry and detection device 742 (Figure 71) is couple on to the shaft of the penetrating member 720. The drive cycle described above may also actuate the module 740 so that it rests at the surface of the finger to acquire blood once the penetrating member retracts from the wound. The module 740 is allowed to remain on the surface of the finger or other tissue site until the gripper 738 has reached the back end 744 of the microfluidics module 740, at which point the module is also retracted into the casing. The amount of time the module 740 remains on the finger, in this embodiment, may be varied based on the distance the end 744 is located and the amount of time it takes the gripper to engage it on the withdrawal stroke. The blood filled module 740, filled while the module remains on pierced tissue site, may then undergo analyte detection by means such as but not limited to optical or electrochemical sensing.
- The blood may be filled in the lumen that the penetrating member was in or the module may have separately defined sample chambers to the side of the penetrating member lumen. The analyte detecting member may also be placed right at the immediate vicinity or slightly setback from the module opening receiving blood so that low blood volumes will still reach the analyte detecting member. In some embodiments, the analyte sensing device and a visual display or other interface may be on board the apparatus and thus provide a readout of analyte levels without need to plug apparatus or a test strip into a separate reader device. As seen in Figure 71, the cover 746 may also be clear to allow for light to pass through for optical sensing. The analyte detecting member may be used with low volumes such as less than about 1 microliter of sample, preferably less than about 0.6 microliter, more preferably less than about 0.3 microliter, and most preferably less than about 0.1 microliter of sample.
- In another embodiment as seen in Figure 72, sensing elements 760 may be directly printed or formed on the top or bottom of the penetrating member cartridge 700, depending on orientation. The bare penetrating member 720 is then actuated through a hole 762 in the plastic facing, withdrawn into the radial cavity followed by the blood

sample. Electrochemical or optical detection for analyte sensing may then be carried out (Figure 72). Again the cavity 766 may have a clear portion to allow light to pass for optical sensing. In one embodiment, a multiplicity of miniaturized analyte detecting member fields may be placed on the floor of the radial cavity as shown in Figure 72 or on 5 the microfluidic module shown in Figure 71 to allow many tests on a single analyte form a single drop of blood to improve accuracy and precision of measurement. Although not limited in this manner, additional analyte detecting member fields or regions may also be included for calibration or other purposes.

Referring now to Figure 73, a still further embodiment of a cartridge according to 10 the present invention will be described. Figure 73 shows one embodiment of a cartridge 800 which may be removably inserted into an apparatus for driving penetrating members to pierce skin or tissue. The cartridge 800 has a plurality of penetrating members 802 that may be individually or otherwise selectively actuated so that the penetrating members 802 may extend outward from the cartridge, as indicated by arrow 804, to penetrate tissue. In 15 the present embodiment, the cartridge 800 may be based on a flat disc with a number of penetrating members such as, but in no way limited to, (25, 50, 75, 100, ...) arranged radially on the disc or cartridge 800. It should be understood that although the cartridge 800 is shown as a disc or a disc-shaped housing, other shapes or configurations of the cartridge may also work without departing from the spirit of the present invention of 20 placing a plurality of penetrating members to be engaged, singly or in some combination, by a penetrating member driver.

Each penetrating member 802 may be contained in a cavity 806 in the cartridge 800 with the penetrating member's sharpened end facing radially outward and may be in the same plane as that of the cartridge. The cavity 806 may be molded, pressed, forged, 25 or otherwise formed in the cartridge. Although not limited in this manner, the ends of the cavities 806 may be divided into individual fingers (such as one for each cavity) on the outer periphery of the disc. The particular shape of each cavity 806 may be designed to suit the size or shape of the penetrating member therein or the amount of space desired for placement of the analyte detecting members 808. For example and not limitation, the 30 cavity 806 may have a V-shaped cross-section, a U-shaped cross-section, C-shaped cross-section, a multi-level cross section or the other cross-sections. The opening 810 through which a penetrating member 802 may exit to penetrate tissue may also have a variety of shapes, such as but not limited to, a circular opening, a square or rectangular opening, a

U-shaped opening, a narrow opening that only allows the penetrating member to pass, an opening with more clearance on the sides; a slit, a configuration as shown in Figure 75, or the other shapes.

In this embodiment, after actuation, the penetrating member 802 is returned into the cartridge and may be held within the cartridge 800 in a manner so that it is not able to be used again. By way of example and not limitation, a used penetrating member may be returned into the cartridge and held by the launcher in position until the next lancing event. At the time of the next lancing, the launcher may disengage the used penetrating member with the cartridge 800 turned or indexed to the next clean penetrating member such that the cavity holding the used penetrating member is position so that it is not accessible to the user (i.e. turn away from a penetrating member exit opening). In some embodiments, the tip of a used penetrating member may be driven into a protective stop that hold the penetrating member in place after use. The cartridge 800 is replaceable with a new cartridge 800 once all the penetrating members have been used or at such other time or condition as deemed desirable by the user.

Referring still to the embodiment in Figure 73, the cartridge 800 may provide sterile environments for penetrating members via seals, foils, covers, polymeric, or similar materials used to seal the cavities and provide enclosed areas for the penetrating members to rest in. In the present embodiment, a foil or seal layer 820 is applied to one surface of the cartridge 800. The seal layer 820 may be made of a variety of materials such as but not limited to a metallic foil or other seal materials and may be of a tensile strength and other quality that may provide a sealed, sterile environment until the seal layer 820 is penetrate by a suitable or penetrating device providing a preselected or selected amount of force to open the sealed, sterile environment. Each cavity 806 may be individually sealed with a layer 820 in a manner such that the opening of one cavity does not interfere with the sterility in an adjacent or other cavity in the cartridge 800. As seen in the embodiment of Figure 73, the seal layer 820 may be a planar material that is adhered to a top surface of the cartridge 800.

Depending on the orientation of the cartridge 800 in the penetrating member driver apparatus, the seal layer 820 may be on the top surface, side surface, bottom surface, or other positioned surface. For ease of illustration and discussion of the embodiment of Figure 73, the layer 820 is placed on a top surface of the cartridge 800. The cavities 806 holding the penetrating members 802 are sealed on by the foil layer 820

and thus create the sterile environments for the penetrating members. The foil layer 820 may seal a plurality of cavities 806 or only a select number of cavities as desired.

In a still further feature of Figure 73, the cartridge 800 may optionally include a plurality of analyte detecting members 808 on a substrate 822 which may be attached to a bottom surface of the cartridge 800. The substrate may be made of a material such as, but not limited to, a polymer, a foil, or other material suitable for attaching to a cartridge and holding the analyte detecting members 808. As seen in Figure 73, the substrate 822 may hold a plurality of analyte detecting members, such as but not limited to, about 10-50, 50-100, or other combinations of analyte detecting members. This facilitates the assembly and integration of analyte detecting members 808 with cartridge 800. These analyte detecting members 808 may enable an integrated body fluid sampling system where the penetrating members 802 create a wound tract in a target tissue, which expresses body fluid that flows into the cartridge for analyte detection by at least one of the analyte detecting members 808. The substrate 822 may contain any number of analyte detecting members 808 suitable for detecting analytes in cartridge having a plurality of cavities 806. In one embodiment, many analyte detecting members 808 may be printed onto a single substrate 822 which is then adhered to the cartridge to facilitate manufacturing and simplify assembly. The analyte detecting members 808 may be electrochemical in nature. The analyte detecting members 808 may further contain enzymes, dyes, or other detectors which react when exposed to the desired analyte. Additionally, the analyte detecting members 808 may comprise of clear optical windows that allow light to pass into the body fluid for analyte analysis. The number, location, and type of analyte detecting member 808 may be varied as desired, based in part on the design of the cartridge, number of analytes to be measured, the need for analyte detecting member calibration, and the sensitivity of the analyte detecting members. If the cartridge 800 uses an analyte detecting member arrangement where the analyte detecting members are on a substrate attached to the bottom of the cartridge, there may be through holes (as shown in Figure 76), wicking elements, capillary tube or other devices on the cartridge 800 to allow body fluid to flow from the cartridge to the analyte detecting members 808 for analysis. In other configurations, the analyte detecting members 808 may be printed, formed, or otherwise located directly in the cavities housing the penetrating members 802 or areas on the cartridge surface that receive blood after lancing.

The use of the seal layer 820 and substrate or analyte detecting member layer 822 may facilitate the manufacture of these cartridges 10. For example, a single seal layer 820 may be adhered, attached, or otherwise coupled to the cartridge 800 as indicated by arrows 824 to seal many of the cavities 806 at one time. A sheet 822 of analyte detecting members may also be adhered, attached, or otherwise coupled to the cartridge 800 as indicated by arrows 825 to provide many analyte detecting members on the cartridge at one time. During manufacturing of one embodiment of the present invention, the cartridge 800 may be loaded with penetrating members 802, sealed with layer 820 and a temporary layer (not shown) on the bottom where substrate 822 would later go, to provide a sealed environment for the penetrating members. This assembly with the temporary bottom layer is then taken to be sterilized. After sterilization, the assembly is taken to a clean room (or it may already be in a clear room or equivalent environment) where the temporary bottom layer is removed and the substrate 822 with analyte detecting members is coupled to the cartridge as shown in Figure 73. This process allows for the sterile assembly of the cartridge with the penetrating members 802 using processes and/or temperatures that may degrade the accuracy or functionality of the analyte detecting members on substrate 822. As a nonlimiting example, the entire cartridge 800 may then be placed in a further sealed container such as but not limited to a pouch, bag, plastic molded container, etc...to facilitate contact, improve ruggedness, and/or allow for easier handling.

In some embodiments, more than one seal layer 820 may be used to seal the cavities 806. As examples of some embodiments, multiple layers may be placed over each cavity 806, half or some selected portion of the cavities may be sealed with one layer with the other half or selected portion of the cavities sealed with another sheet or layer, different shaped cavities may use different seal layer, or the like. The seal layer 820 may have different physical properties, such as those covering the penetrating members 802 near the end of the cartridge may have a different color such as but not limited to red to indicate to the user (if visually inspectable) that the user is down to say 10, 5, or other number of penetrating members before the cartridge should be changed out.

Referring now to Figures 74 and 75, one embodiment of the microfluidics used with the analyte detecting members 808 in cartridge 800 will now be described. For ease of illustration, the shape of cavity 806 has been simplified into a simple wedge shape. It

should be understood that more sophisticated configurations such as but not limited to that shown in Figure 73 may be used. Figure 74 shows a channel 826 that assists in drawing body fluid towards the analyte detecting members 808. In the present embodiment, two analyte detecting members 808 are shown in the cavity 806. This is purely for illustrative purposes as the cavity 806 may have one analyte detecting member or any other number of analyte detecting members as desired. Body fluid entering cavity 806, while filling part of the cavity, will also be drawn by capillary action through the groove 826 towards the analyte detecting members 808. The analyte detecting members 808 may all perform the same analysis, they may each perform different types of analysis, or there may be some combination of the two (some sensors perform same analysis while others perform other analysis).

Figure 75 shows a perspective view of a cutout of the cavity 806. The penetrating member 802 (shown in phantom) is housed in the cavity 806 and may extend outward through a penetrating member exit opening 830 as indicated by arrow 832. The position of the tip of penetrating member 802 may vary, such as but not limited to being near the penetrating member exit port or spaced apart from the exit. The location of the tip relative to the analyte detecting member 808 may also be varied, such as but not limited to being spaced apart or away from the analyte detecting member or collocated or in the immediate vicinity of the analyte detecting member. Fluid may then enter the cavity 806 and directed by channel 826. The channel 826 as shown in Figure 75 is a groove that is open on top. The channel 826 may be entirely a groove with an open top or it may have a portion that has a sealed top forming a lumen, or still further, the groove may be closed except for an opening near the penetrating member exit opening 830. It should be understood that capillary action can be achieved using a groove having one surface uncovered. In some embodiments, the analyte detecting member 808 is positioned close to the penetrating member exit opening 830 so that the analyte detecting member 808 may not need a capillary groove or channel to draw body fluid, such as in Figure 78.

As seen in Figures 75 and 76, the cavity 806 may include the substrate 822 coupled to its bottom surface containing the analyte detecting members 808. With the analyte detecting members 808 located on the underside of the cartridge 800 as seen in the embodiment of Figure 76, the cartridge 800 may include at least one through hole 834 to provide a passage for body fluid to pass from the cavity 806 to the analyte detecting member 808. The size, location, shape, and other features of the through hole 834 may be

varied based on the cavity 806 and number of analyte detecting members 808 to be provided. In other embodiments, wicking elements or the like may be used to draw body fluid from the groove 826 to down to the analyte detecting member 808 via the through hole or holes 834.

- 5 Referring now to Figure 77, a variety of groove and analyte detecting member configurations are shown on a single cartridge. These configurations are shown only for illustrative purposes and a single cartridge may not incorporate each of these configurations. Some embodiments may use any of the detecting members, singly or in combination. It should be understood, however, that analyte detecting member
10 configuration could be customized for each cavity, such as but not limited to, using a different number and location of analyte detecting members depending lancing variables associated with that cavity, such as but not limited to, the time of day of the lancing event, the type of analyte to be measured, the test site to be lanced, stratum corneum hydration, or other lancing parameter. As a nonlimiting example, the detecting members may be
15 moved closer towards the outer edge of the disc, more on the side walls, any combination, or the like.

Figure 77 shows a penetrating member 802 in a cavity 838 with three analyte detecting members 808 in the cavity. For ease of illustration, the penetrating member 802 is omitted from the remaining cavities so that the analyte detecting member
20 configurations can be more easily seen. Cavity 840 has a channel 826 with two analyte detecting members 808. Cavity 842 has a channel 844 coupled to a single analyte detecting member 808. Cavities 846 and 848 have one and two analyte detecting members 808, respectively. The analyte detecting members 808 in those cavities may be located directly at the penetrating member exit from the cartridge or substantially at the
25 penetrating member exit. Other analyte detecting member configurations are also possible, such as but not limited to, placing one or more analyte detecting members on a side wall of the cavity, placing the analyte detecting members in particular arrays (for example, a linear array, triangular array, square array, etc...) on the side wall or bottom surface, using mixed types of analyte detecting members (for example, electrochemical
30 and optical, or some other combination), or mixed positioning of analyte detecting members (for example, at least one analyte detecting member on the substrate below the cartridge and at least one analyte detecting member in the cavity).

Figure 78 shows an embodiment of cartridge 800 where the analyte detecting member 850 is located near the distal end of cavity 806. The analyte detecting member 850 may be formed, deposited, or otherwise attached there to the cartridge 800. In another embodiment, the analyte detecting member 850 may be a well or indentation having a bottom with sufficient transparency to allow an optical analyte detecting member to detect analytes in fluid deposited in the well or indentation. The well or indentation may also include some analyte reagent that reacts (fluoresces, changes colors, or presents other detectable qualities) when body fluid is placed in the well. In a still further embodiment, analyte detecting member 850 may be replaced with a through hole that allow fluid to pass there through. An analyte detecting member 808 on a substrate 822 may be attached to the underside of the cartridge 800, accessing fluid passing from the cavity 806 down to the analyte detecting member 808.

As mentioned above, the analyte detecting members 808 may also be placed right at the immediate vicinity or slightly setback from the module opening receiving blood so that low blood volumes will still reach the analyte detecting member. The analyte detecting members 808 may be used with low volumes such as less than about 1 microliter of sample, preferably less than about 0.6 microliter, more preferably less than about 0.3 microliter, and most preferably less than about 0.1 microliter of sample. Analyte detecting members 808 may also be directly printed or formed on the bottom of the penetrating member cartridge 800. In one embodiment, a multiplicity of miniaturized analyte detecting member fields may be placed on the floor of the radial cavity or on the microfluidic module to allow many tests on a single analyte form a single drop of blood to improve accuracy and precision of measurement. Although not limited in this manner, additional analyte detecting member fields or regions may also be included for calibration or other purposes.

Referring now to Figures 79-84, further embodiments of the cartridge 800 will now be described. Figure 79 shows a cartridge 860 having a half-circular shape. Figure 80 shows a cartridge 862 in the shape of a partial curve. Figure 80 also shows that the cartridges 862 may be stacked in various configurations such as but not limited to vertically, horizontally, or in other orientations. Figure 81 shows a cartridge 864 having a substantially straight, linear configuration. Figure 82 shows a plurality of cartridges 864 arranged to extend radially outward from a center 866. Each cartridge may be on a slide (not shown for simplicity) that allows the cartridge 864 to slide radially outward to be

aligned with a penetrating member launcher. After use, the cartridge 864 is slide back towards the center 866 and the entire assembly is rotated as indicated by arrow 868 to bring a new cartridge 864 into position for use with a penetrating member driver. Figure 83 shows a still further embodiment where a plurality of cartridges 800 may be stacked 5 for use with a penetrating member driver (see Figure 85). The driver may be moved to align itself with each cartridge 800 or the cartridges may be moved to alight themselves with the driver. Figure 84 shows a still further embodiment where a plurality of cartridge 864 are coupled together with a flexible support to define an array. A roller 870 may be used to move the cartridges 864 into position to be actuated by the penetrating member 10 driver 872.

Referring now to Figure 85, one embodiment of an apparatus 880 using a radial cartridge 800 with a penetrating member driver 882 is shown. A contoured surface 884 is located near a penetrating member exit port 886, allowing for a patient to place their finger in position for lancing. Although not shown, the apparatus 880 may include a 15 human readable or other type of visual display to relay status to the user. The display may also show measured analyte levels or other measurement or feedback to the user without the need to plug apparatus 880 or a separate test strip into a separate analyte reader device. The apparatus 880 may include a processor or other logic for actuating the penetrating member or for measuring the analyte levels. The cartridge 800 may be loaded 20 into the apparatus 880 by opening a top housing of the apparatus which may be hinged or removably coupled to a bottom housing. The cartridge 800 may also drawn into the apparatus 880 using a loading mechanism similar in spirit to that found on a compact disc player or the like. In such an embodiment, the apparatus may have a slot (similar to a CD player in an automobile) that allows for the insertion of the cartridge 800 into the 25 apparatus 880 which is then automatically loaded into position or otherwise seated in the apparatus for operation therein. The loading mechanism may be mechanically powered or electrically powered. In some embodiments, the loading mechanism may use a loading tray in addition to the slot. The slot may be placed higher on the housing so that the cartridge 800 will have enough clearance to be loaded into the device and then dropped 30 down over the penetrating member driver 882. The cartridge 800 may have an indicator mark or indexing device that allows the cartridge to be properly aligned by the loading mechanism or an aligning mechanism once the cartridge 800 is placed into the apparatus 880. The cartridge 800 may rest on a radial platform that rotates about the penetrating

member driver 882, thus providing a method for advancing the cartridge to bring unused penetrating members to engagement with the penetrating member driver. The cartridge 800 on its underside or other surface, may shaped or contoured such as but not limited to with notches, grooves, tractor holes, optical markers, or the like to facilitate handling and/or indexing of the cartridge. These shapes or surfaces may also be varied so as to indicate that the cartridge is almost out of unused penetrating members, that there are only five penetrating members left, or some other cartridge status indicator as desired.

5 A suitable method and apparatus for loading penetrating members has been described previously in commonly assigned, copending U.S. patent applications Attorney 10 Docket 38187-2589 and 38187-2590, and are included here by reference for all purposes. Suitable devices for engaging the penetrating members and for removing protective materials associated with the penetrating member cavity are described in commonly 15 assigned, copending U.S. patent applications Attorney Docket 38187-2601 and 38187-2602, and are included here by reference for all purposes. For example in the embodiment of Figure 78, the foil or seal layer 820 may cover the cavity by extending across the cavity along a top surface 890 and down along the angled surface 892 to provide a sealed, sterile environment for the penetrating member and analyte detecting members therein. A piercing element described in U.S. patent applications Attorney 20 Docket 38187-2602 has a piercing element and then a shaped portion behind the element which pushes the foil to the sides of the cavity or other position so that the penetrating member 802 may be actuated and body fluid may flow into the cavity.

Referring now to Figure 86, a still further embodiment of a lancing system according to the present invention will be described. A radial cartridge 500 may be incorporated for use with a penetrating member driver 882. A penetrating member may 25 be driven outward as indicated by arrow 894. A plurality of analyte detecting members are presented on a roll 895 that is laid out near a penetrating member exit. The roll 895 may be advanced as indicated by arrow 896 so that used analyte detecting members are moved away from the active site. The roll 895 may also be replaced by a disc holding a plurality of analyte detecting members, wherein the analyte detecting member disc (not 30 shown) is oriented in a plane substantially orthogonal to the plane of cartridge 500. The analyte detecting member disc may also be at other angles not parallel to the plane of cartridge 500 so as to be able to rotate and present new, unused analyte detecting member in sequence with new unused penetrating members of cartridge 500.

Referring now to Figure 87A, the cartridge 500 provides a high density packaging system for a lancing system. This form factor allows a patient to load a large number penetrating members through a single cartridge while maintaining a substantially handheld device. Of course such a cartridge 500 may also be used in non-handheld devices. The present cartridge 500 provide a high test density per volume of the disposable. For embodiments of a cartridge that includes analyte detecting members in addition to penetrating members such as cartridge 800, the density may also be measured in terms of density of analyte detecting members and penetrating members in a disposable. In other embodiments, the density may also be expressed in terms of analyte detecting members per disposable. For example, by taking the physical volume of one embodiment or the total envelope, this number can be divided by the number of penetrating members or number of tests. This result is the volume per penetrating member or per test in a cassetted fashion. For example, in one embodiment of the present invention, the total volume of the cartridge 500 is determined to be 4.53 cubic centimeters. In this one embodiment, the cartridge 500 holds 50 penetrating members. Dividing the volume by 50, the volume per test is arrived at 0.090 cubic centimeters. Conventional test devices such as drum is in the range of 0.720 or 0.670 cubic centimeters and that is simply the volume to hold a plurality of test strips. This does not include penetrating members as does the present embodiment 800. Thus, the present embodiment is at a substantially higher density. Even a slightly lower density device having penetrating members and analyte detecting members in the 0.500 cubic centimeter range would be a vast improvement over known devices since the numbers listed above for known devices does not include penetrating members, only packaging per test strip.

Each penetrating member (or penetrating member and analyte detecting member, as the case may be) may have a packing density, or occupied volume, in cartridge 500. In various embodiments, the packing density or occupied volume of each penetrating member in cartridge 500 may be no more than about 0.66 cm³, 0.05 cm³, 0.4 cm³, 0.3 cm³, 0.2 cm³, 0.1 cm³, 0.075 cm³, 0.05 cm³, 0.025 cm³, 0.01 cm³, 0.090 cm³, 0.080 cm³, and the like. These numbers applicable to volumes for penetrating members alone, for combined-penetrating members and analyte detecting members, and/or just analyte detecting members. In other words, the volume required for each penetrating member does not exceed 0.66 cm³/penetrating member, 0.05 cm³/penetrating member, 0.4 cm³/penetrating member, 0.3 cm³/penetrating member, 0.2 cm³/penetrating member, 0.1

cm³/penetrating member, 0.075 cm³/penetrating member, 0.05 cm³/penetrating member, 0.025 cm³/penetrating member, 0.01 cm³/penetrating member, 0.090 cm³/penetrating member and the like. So, if the total package volume of the cartridge is defined as X and the cartridge includes Y number of penetrating members, penetrating members and test area, or other unit 395, the volume for each unit does not exceed 0.66 cm³, 0.05 cm³, 0.4 cm³, 0.3 cm³, 0.2 cm³, 0.1 cm³, 0.075 cm³, 0.05 cm³, 0.025 cm³, 0.01 cm³, 0.090 cm³, 0.080 cm³, and the like.

Referring now to Figure 87B, a still further embodiment of a cartridge according to the present invention will now be described. Figure 87B shows a cross-section of a 10 conical shaped cartridge with the penetrating member being oriented in one embodiment to move radially outward as indicated by arrow 897. In another embodiment, the penetrating member may be oriented to move radially inward as indicated by arrow 895. The gripper may be positioned to engage the penetrating member from an inner surface or an outer surface of the cartridge.

15 Referring now to Figure 88, nanowires may also be used to create low volume analyte detecting members used with the cartridge 800. Further details of a nanowire device is described in commonly assigned, copending U.S. Provisional Patent Application Ser. No. 60/433,286 (Attorney Docket No. 38187-2605) filed December 13, 2002, fully incorporated herein by reference for all purposes. These nanowire analyte detecting members 898 may be incorporated into the cavity 806 housing the penetrating member 802. They may be placed on the floor or bottom surface of the cavity 806, on the wall, on 20 the top surface, or any combinations of some or all of these possibilities. The analyte detecting members 898 may be designed to have different sensitivity ranges so as to enhance the overall sensitivity of an array of such analyte detecting members. Methods to achieve this may include, but are not limited to, using nanowires of varying sizes, 25 varying the number of nanowires, or varying the amount of glucose oxidase or other glucose detection material on the nanowires. These nanowire analyte detecting members may be designed to use low volumes of body fluid for each sample, due to their size. In some embodiments, each of the analyte detecting members are accurate using volumes of 30 body fluid sample less than about 500 nanoliters. In some embodiments, each of the analyte detecting members are accurate using volumes of body fluid sample less than about 300 nanoliters. In still other embodiments, each analyte detecting member is accurate with less than about 50 nanoliters, less than about 30 nanoliters, less than about

10 nanoliters, less than about 5 nanoliters, and less than about 1 nanoliters of body fluid sample. In some embodiments, the combined array of analyte detecting members uses less than 300 nanoliters of body fluid to arrive at an analyte measurement.

Referring now to Figure 89, a still further embodiment of the present invention will be described. Figure 89 shows one embodiment of an optical illumination system 910 for use with optical analyte detecting members (Figure 91) that may be in contact with a body fluid sample. The overall system may include a plurality of analyte detecting members which provide some optical indicator, a light source 912 for providing light to shine on the analyte detecting members, at least one light detector 914, and a processor (not shown). The analyte detecting member or analyte detecting members are exposed to a sample of the fluid of unknown composition. A plurality of analyte detecting members may be arranged into an array of analyte detecting members exposed to one fluid sample, each group targeting a specific analyte and may contain an analyte-specific chemical that interacts more specifically with one analyte than with some other analytes to be analyzed. Each analyte detecting member may also have different sensitivity ranges so as to maximize overall sensitivity of an array of such analyte detecting members. The light source 912 shines light on at least one analyte detecting member to cause light interaction. The differences in the analyte detecting members may lead to differences in the light interaction. The light detector detects the light interaction by the analyte detecting members. The processor analyzes the light interaction by the analyte detecting members to take into account interference in light interaction among the analytes, thereby determining the concentration of the desired analyte in the fluid.

Referring still to the embodiment of Figure 89, the light source 912 may be but is not limited to an LED. An alternative LED 915 may also be used with the present invention. Light, illumination, or excitation energy from LED 912 travels along a path through a pinhole 916, a filter 917, and a lens 918. The light then comes into contact with a beamsplitter 919 such as but not limited to a dichroic mirror or other device useful for beamsplitting. The light is then directed towards lens 920 as indicated by arrow 921. The lens 920 focuses light onto the analyte detecting member (Figure 91). This excitation energy may cause a detectable optical indicator from the analyte detecting member. By way of example and not limitation, fluorescence energy may be reflected back up the lens 920. This energy passes through the beamsplitter 919 and to lens 922 which is then received by detector 914 as indicated by arrow 923. The detector 914 measures the

energy and this information is passed on to the processor (not shown) to determine analyte levels. The illumination system 910 may also include cells 924 on the disc surface. In this specific embodiment, a penetrating member 925 driven by a force generator 926 such as but not limited to a solenoid may be used to obtain the fluid sample. A detent 927 may also be included with the device along with other bare lancets or penetrating members 928.

Referring now to Figure 90, another embodiment of the illumination system 910 is shown for use with a cartridge 929. Cartridge 929 is similar to cartridge 800. Cartridge 929 is a single cartridge having a plurality of penetrating members and a plurality of optical analyte detecting members (not shown). The cartridge 929 further includes a plurality of optically transparent portions 930 which may be but is not limited to windows or the like for the light from LED 912 to shine into a cavity of the cartridge 929. In one embodiment, each cavity of the cartridge 929 may include at least one transparent portion 930. This allows the light to generate energy that may be read by analyte detecting member 914. The cartridge 929 may be used a driver 882 to actuate penetrating members and the cartridge 929 may rotate as indicated by arrow 931.

Referring now to Figure 91, a cross-section of a similar embodiment of the illumination system is shown. This system 932 has source 912 with a lens 933 having an excitation filter 934. This excitation filter 934, in one embodiment, only allows excitation energy to pass. This filter 934 allows the excitation energy to pass to dichroic mirror 935, but does not let it return to source 912. Excitation energy is reflected down as indicated by arrow 936. Lens 937 focuses the energy to optical analyte detecting member 938. Fluorescence energy 939 passes through the dichroic mirror 935 and towards a fluorescent filter 940. In one embodiment, the fluorescent filter 940 only allows 25 fluorescent energy to pass through to lens 941. Thus, the detector 914 only receives fluorescent energy from the analyte detecting member 938. It should be understood of course, that the filter may be changed to allow the type of energy being generated by analyte detecting member 938 to pass. In some embodiments, no filter may be used. The dichroic mirror 935 may be a Bk7 substrate, 63x40x8mm. The filters may also be a Bk7 substrate about 40mm in diameter and about 6mm thick. The lens 933, 937, and 941 may be achromatic: bfl=53.6, working aperture 38mm.

Referring now to Figure 92, a still further embodiment of an illumination system 942 will be described. This system does not use a beamsplitter or dichroic mirror.

Instead, both the source or LED 912 and detector 914 have direct line of sight to the optical analyte detecting member 938. In this embodiment, multiple elements are combined into a single housing. For example, lens 943, lens 944, and filter 945 are combined while lens 946, lens 947, and filter 948 are also combined.

5 Referring now to Figure 93, a cross-section of a system similar to that of Figure 89 is shown in a housing 950. LED 912 sends light to mirror 919 to a light path 951 to cells 924 on a surface of the disc. A finger access 952 allows a sample to be obtained and flow along a fluid pathway 953 to be analyzed. A processor 954 may be coupled to detector 914 to analyze the results.

10 Referring now to Figure 94, a cross-section of a system similar to that of Figure 90 will be further described. This shows a cartridge 929 used with a driver 882. This allows for a radial design where the penetrating members extend radially outward as indicated by arrow 955. The driver 882 may have a coupler portion that reciprocates as indicated by arrow 956. Figures 95 and 96 provide further views of a system similar to 15 that of Figure 89. The embodiment of Figures 95 and 96 may include additional lenses or filters as may be useful to refine energy detection.

Referring now to Figure 97, the area of interest is the velocity profile 1000 while the lancet is cutting through the skin layers in the finger until it reaches a predetermined depth. More specifically, variation of lancet velocity through different phases of the 20 inbound trajectory is shown in Figure 97. In this embodiment, Phase I corresponds to the stratum corneum, phase II to the epidermis and phase III to the dermis. At each phase (and during the phase), the options are to maintain current velocity, increase current velocity or decrease current velocity. Based on the thickness of the stratum corneum, velocity could be monitored and changed in this embodiment at 9 points in the stratum 25 corneum, 6 points in the epidermis, and 29 points in the dermis using the four edge detection algorithm and the 360 strips per inch encoder strip. It should be noted that although the embodiment of the driver discussed herein produces the previously discussed number of monitoring points for a given displacement, other driver and position sensor embodiments may be used that would give higher or lower resolution.

30 For the purposes of the present discussion for this nonlimiting example, the skin is viewed as having three distinct regions or tissue layers: the stratum corneum SC (Phase I), the epidermis E (Phase II) and the dermis D (Phase III). In one embodiment, the lancet or penetrating member 10 is accelerated to a first desired velocity. This velocity may be

predetermined or it may be calculated by the processor during actuation. The processor is also used to control the lancet velocity in tissue. At this velocity, the lancet 10 will impact the skin and initiate cutting through the stratum corneum. The stratum corneum is hard, hence in this embodiment, maximum velocity of the penetrating member 10 may be 5 employed to efficiently cut through this layer, and this velocity may be maintained constant until the lancet passes through the layer. Power will likely need to be applied to the lancet drive 12 while the lancet is cutting through the stratum corneum in order to maintain the first velocity. Average stratum corneum thickness is about 225 μm . Using a four-edge detection algorithm for the position sensor 14 of this embodiment, the 10 opportunity to verify and feed back velocity information can be carried out at 225/17 or roughly 13 points. In another embodiment accelerating through the stratum corneum following impact may improve cutting efficiency. Acceleration may be possible if the lancet has not reached its target or desired velocity before impact. Figure 4 shows the 15 result of increasing ((a) arrows, maintaining ((b) arrows) or reducing ((c) arrows) velocity on the lancet trajectory for each of the tissue layers.

On reaching the epidermis E (Phase II), an embodiment of a method may decrease the velocity ((c) arrows) from the first velocity so that tissue compression is reduced in this second tissue layer. Thus the lancet 10, in this nonlimiting example, may have a second desired velocity that is less than the first velocity. The reduced speed in the 20 second tissue layer may reduce the pain experienced by the mechano receptor nerve cells in the dermal layer (third tissue layer). In the absence of tissue compression effects on the dermal layer, however, lancet velocity may be kept constant for efficient cutting (i.e. second velocity may be maintained the same as the first velocity). In another embodiment, velocity may be increased in the second tissue layer from the first velocity.

25 In Phase III, the lancet or penetrating member 10 may reach the blood vessels and cut them to yield blood. The innervation of this third tissue layer and hence pain perception during lancing could be easily affected by the velocity profile chosen. In one embodiment, a third desired velocity may be chosen. The velocity may be chosen to minimize nerve stimulation while maintaining cutting efficiency. One embodiment 30 would involve reducing velocity from the second velocity to minimize pain, and may increase it just before the blood vessels to be cut. The number of velocity measurement steps possible for the position sensor described above in the dermis is approximately 58. The user would determine the best velocity/cutting profile by usage. The profile with the

least amount of pain on lancing, yielding a successful blood sample would be programmable into the device.

Currently users optimize depth settings on mechanical launchers by testing various settings and through usage, settle on a desired setting based on lancing comfort.

- 5 Embodiments of the device and methods discussed herein provide a variety of velocity profiles (Figure 97), which can be optimized by the user for controlled lancing, and may include: controlling the cutting speed of a lancet with the lancet within the skin; adjusting the velocity profile of the lancet while the lancet is in the skin based upon the composition of the skin layers; lancing according to precise regional velocity profiles
- 10 based on variation in cell type from the surface of the skin down through the epidermis and dermis; lancing at a desired velocity through any tissue layer and varying the velocity for each layer. This may include maximum velocity through the stratum corneum, mediation of velocity through epidermis to minimize shock waves to pain sensors in dermis, and mediation of velocity through dermis for efficient cutting of blood
- 15 vessels without stimulating pain receptors. Additional details may be found in commonly assigned, co-pending U.S. Patent Application Ser. No. 10/420,535 (Attorney Docket No. 38187-2664) filed April 21, 2003, included herein by reference.

Referring now to Figure 98, another embodiment of the present invention will now be described. Some embodiments of the present invention may provide an accurate method to locate the point on the body where the sample will be taken. As a nonlimiting example, a beam of light may be used. Additionally, the beam may be used to indicate readiness to sample. In a still further embodiment, the reflected light beam may be used to arm the device for use or to actually activate the device. Any of these embodiments may be designed for use with any of the cartridges and/or lancing systems described herein.

As seen in the embodiment of Figure 98, a light source 1000 may be used to project a light beam on to the surface of the skin or tissue. A variety of light sources may be used. The light source include but are not limited to an incandescent, light emitting diode, fluorescent, electroluminescent or other type of light sources. The light source 1000, in most embodiments, emits radiation in the spectrum visible to the human eye. The light source 1000 may also emit radiation at other wavelengths such as but not limited to ultraviolet, infrared, or the like and would be detected by a separate detector device. One example may be similar to the device of Figure 99. Although the

embodiment of Figure 98 uses a plurality of light sources 1000, it should be understood that some embodiments may only use a single light source 1000.

In the embodiment of Figure 98, an element may be provided to guide the light to the target area of the body. This may be accomplished by using a light source with a built 5 in collimating means such as but not limited to a lens. Another way to guide the light is to allow it to escape through one or more apertures 1002 in the device. An end cap or front end 103 may be provided to facilitate finger positioning. A still further way is to use a form of fiber optics or light pipe technology that makes a beam of light on the body. The light pipe technology may have lenses (such as, but not limited to, conventional or 10 Fresnel) built into them. As seen in Figure 98, the lancet or penetrating member 1004 exits through an opening 1006. The device may include a coupler 1008 attaching a driver to the penetrating member 1004. Wires or leads 110 may be used to deliver power to drive the light source 1000. It should be understood that the number of light beams may vary. The light beams may be one, two, or more individual beams or a continuous ring or 15 other shape of light (such as but limited to a circle, a dot, an X, an icon, an logo, etc...) to mark the point of impact. The light source 1000 may also project different color of light. As a nonlimiting example, a first color of light may be used for targeting, and a second color of light when the device is aimed correct or at a desired target. For example, a red light may be used initially and a green light when the device is accurately targeted. Two 20 different light sources 1000 may be used to provide the different colors of light.

Referring now to Figure 99, an additional feature could allow a photo diode or similar sensor 1020 to detect the reflected light from the source 1000, which may be used for a variety of purposes such as arming the device for actuation, determining skin characteristics, or using the reflected signal to initiate the lancing operation. In the 25 embodiment of Figure 99, fiber optics 1022 may be used to carry light from the source 1000 for projection. In one embodiment, the light beam may be modulated at a fairly high frequency that may enhance the detection process, by detecting an AC coupled detector signal. The reflection of the location light beam may be used to detect proximity of the anatomical feature. Modulation provides one method to reject ambient light levels 30 that would falsely indicate proximity of the anatomical feature. The light is projected to a point of sampling S, where the lancet or penetrating if actuated, will create a wound.

There are additional uses for the light source 1000 – the light may be used with an electronic actuator to indicate that the device is ready to lance. In addition to the beam

illuminating the site of lancing, the light could be visible within the body of the device as an easy to see ready to use signal. In this case a switch would turn on and off the light source to indicate the status of the device. In another embodiment, a visual indicator 1040 on the device may light up or change color when the device is properly aimed. An 5 indicator, change of image, flashing of black and white on an LCD display screen on the device may also be used to indicate proper aim. In some situations, when the device is aimed over a ridge on the finger (i.e. ridge associated with lines on a finger that creates fingerprints), the light may indicate one color and a second color when the device aimed over a valley or trough between ridges. In some embodiments, a second light beam or 10 second image is projected when the device is aimed as desired. The beam of light may be controlled to indicate readiness for service to the operator. Additionally, the beam may be made visible by a secondary light conduction path (other than the light beam).

Referring now to Figure 100, in this embodiment, it is shown the light source 1000 does not need to be located in front of the cartridge 500. It should be understood 15 that the light source 100 may have an overlapping configuration where the source may be above, below, or to the side of the cartridge. The light source 1000 may be used with a device that only contains one penetrating member 1004 or a device that contains multiple penetrating members. In some embodiments which use a light source 912 for analyte detection or measurement, the light source 912 may also be used to provide a light for 20 aiming purposes via an optical train 1042 such as but not limited to optical fiber, mirrors, or lens. For ease of illustration, the other optical components used for light source 912 to perform its analyte measurement functions are not shown in Figure 100.

Referring now to the embodiments in Figures 100 and 101, a portion 1050 of the housing 1052 may be transparent to facilitate viewing of the finger as it is positioned to 25 be lanced. The embodiment in Figure 101 provides a substantially larger area to be clear while the embodiment in Figure 102 provides a clear area in a round, circular, square, rectangular, polygonal, other shaped window near the lancing location. It should be understood that any of the light beam embodiments, clear housing embodiments, and other features used for aiming may be combined with any of the embodiments disclosed 30 herein or with embodiments in references enclosed herein by reference.

Referring now to Figure 103, a still further embodiment of the present invention will now be described. Figure 103 is an exploded view showing a cartridge 1100, a layer 1102 with a plurality of analyte detecting members 1104, and a sterility barrier 1106. The

- analyte detecting members 1104 on layer 1102 may have leads or connectors 1108 that extend along the layer 1102. In some embodiments, these leads 1108 extend all the way to the inner circumference of the layer 1102. In other embodiments, the leads 1108 may not extend all the way to the inner circumference. As indicated by arrows 1110 and 1112,
- 5 the layer 1102 and sterility barrier 1106 may be coupled to the cartridge 1100 to form a device for use with a lancing apparatus 880. In most embodiments, penetrating members (not shown) are contained in the cartridge 1100 prior to coupling the sterility barrier 1106 to the cartridge 1100. It should be understood that the analyte detecting member 1104 may be a low volume electrochemical analyte detecting member such as but not limited to
- 10 that described in published PCT application WO02/02796 fully incorporated herein by reference. The disposable analyte detecting member may comprise a support material, upon which electrical conductors and an electrode system, comprising a counter electrode and a working electrode formed from a reaction layer, are deposited, a dielectric insulating layer, covering the support material and the electrical conductors, recesses for forming contacts for a potentiostat unit and the electrode system and a bio-component for recognition of the analyte. The reaction layer of the disposable analyte detecting member may comprise a lightly subliming electron-transfer mediator along with an electron-conducting material. The electrode system of the analyte detecting member is covered by a polymeric protective coat. The invention further relates to a method for the
- 15 determination of analytes in a fluid sample, by means of the analyte detecting member, the use of lightly subliming compounds as electron-transfer mediators in an electrochemical sensor for the transfer of electrons from an enzyme to an electron conducting material and the use of the analyte detecting members for the determination of analyte concentrations in body or sample fluids. The analyte detecting member may be
- 20 designed to provide a sufficient reading based on no more than about 600 nanoliters, 500 nanoliters, 400 nanoliters, 300 nanoliters, 200 nanoliters, 100 nanoliters, 50 nanoliters, 25 nanoliters, 20 nanoliters, 15 nanoliters, 10 nanoliters, 5 nanoliters, or lower volume. As a nonlimiting example, the analyte detectors may be sized from 1x1 mm or 0.5x0.5 mm in another embodiment.
- 25 Referring now to the embodiment of Figure 104, a cartridge 1114 is shown wherein cavities 1116 are of extended length and have a penetrating member grip or park area 1118. This area 1118 holds the penetrating member (not shown) in place prior to actuation. It may also be used to hold the penetrating member in place after actuation.

The cartridge 1114 may also have notches 1120 formed along the inner circumference of the cartridge. These notches 1120 may be used for positioning purposes, for purposes of rotating the cartridge, or any combination of the two or other reasons. For non-circular configurations, the notches 1120 are formed along the walls of an opening through the
5 noncircular cartridge.

Figure 105 is an enlarged view of a portion of the cartridge 1114. Along the outer periphery of the cartridge 1114, a chamber 1122 is formed. In one embodiment, blood or other body fluid from a wound created by the lancing will gather in the chamber 1122. A channel 1124 may be present to draw fluid towards an opening 1126. In one
10 embodiment, an analyte detecting member (not shown) may occupy the opening 1126. In some embodiments, the analyte detecting member forms the bottom wall of the opening 1126, instead of occupying the opening 1126. In some embodiments, there are no fluid bearing structures on the underside of the cartridge 1114.

Referring now to the embodiments of Figures 106 and 107, configurations for the
15 underside of the cartridge 1114 are shown. In this embodiment, opening 1126 leads to a fluid channel 1128 on the underside of the cartridge 1114. The channel 1128 may be selected of a length sufficient to contain a volume of blood sufficient to substantially fill the expanded fluid area 1130. As a nonlimiting example, the channel 1128 may be configured to hold at least about 1.5 μ l, 1.4 μ l, 1.3 μ l, 1.2 μ l, 1.1 μ l, 1.0 μ l, 0.9 μ l, 0.8 μ l,
20 0.7 μ l, 0.6 μ l, 0.5 μ l, 0.4 μ l, 0.3 μ l, 0.2 μ l, 0.1 μ l, 0.05 μ l, or 0.01 μ l. As another nonlimiting example, the channel 1128 may also be viewed as holding no more than about 1.5 μ l, 1.4 μ l, 1.3 μ l, 1.2 μ l, 1.1 μ l, 1.0 μ l, 0.9 μ l, 0.8 μ l, 0.7 μ l, 0.6 μ l, 0.5 μ l, 0.4
25 μ l, 0.3 μ l, 0.2 μ l, 0.1 μ l, 0.05 μ l, or 0.01 μ l, prior to the fluid entering the area 1130. In a still further embodiment, the amount of fluid flowing from the channel 1128 into the area
20 1130 will not exceed about 1.5 μ l, 1.4 μ l, 1.3 μ l, 1.2 μ l, 1.1 μ l, 1.0 μ l, 0.9 μ l, 0.8 μ l, 0.7
 μ l, 0.6 μ l, 0.5 μ l, 0.4 μ l, 0.3 μ l, 0.2 μ l, 0.1 μ l, 0.05 μ l, or 0.01 μ l, depending on the amount desired by the various detecting members. The analyte detecting member (not shown), in one embodiment, will occupy or will correspond in location to the area 1130.
When fluid fills the fluid channel 1128 and enters the area 1130, the sudden expansion of
30 width will cause fluid to rush into the area 1130, preferably in a volume sufficient to substantially fill the area or at least in sufficient volume for an analyte detecting member to make a reading. The area 1130 may hold about 1.5 μ l, 1.4 μ l, 1.3 μ l, 1.2 μ l, 1.1 μ l, 1.0

μl, 0.9 μl, 0.8 μl, 0.7 μl, 0.6 μl, 0.5 μl, 0.4 μl, 0.3 μl, 0.2 μl, 0.1 μl, 0.05 μl, or 0.01 μl. In some embodiments, the area 1130 is designed to hold a volume slightly less than the amount of that can be held in the channel 1128 prior to the fluid reaching the area 1130. In one nonlimiting example, this may be about 0.01 μl, 0.05 μl, or 0.1 μl less.

5 A vent 1132 may be fluidly coupled to the expanded fluid area 1130 to handle any overflow of fluid. The vent 1132 reconnects to the cavity 1116 on the other side of the cartridge.

Figures 108 and 109 show a still further embodiment according to the present invention. Figure 108 shows an embodiment where the opening 1134 is moved even closer to the outer periphery of the chamber 1122. Again, in some embodiments, the

10 cartridge 1114 may not have any fluid bearing channels or structures. An analyte detecting member may occupy the opening 1134, form the underside of the opening 1134, or some combination of the two. Figure 108 also shows a groove 1136 for gathering excess material from a sterility barrier 1106. Figure 109 shows an embodiment where the opening 1134 opens directly into expanded area 1138. There is no channel to bring the

15 fluid to the expanded area 1138. In this embodiment, three analyte detecting members 1140, 1142, and 1144 may be associated with each area 1138. In any of the embodiments of the present invention, it should be understood that a single or a plurality of analyte detecting members may be associated with each area, such as area 1138. In any of the embodiments of the present invention, it should be understood that the analyte detecting

20 members may be performing the same analysis, different analysis, or any combination thereof.

Referring now to the embodiment of Figure 110, a rib 1146 is positioned across the opening 1148 in the chamber 1150. The chamber 1150 is positioned to receive body fluid from a wound created by the lancing event. The rib 1146 may be formed from a variety of materials such as, but not limited to, a cyclic olefin or other plastic well known in the art. In some embodiments, it can be made hydrophilic by surface treatments or the surrounding area can be made hydrophobic. In one embodiment, the rib 1146 may be made very thin, on the order of about 100 microns. The rib 1146 may also have other thicknesses such as less than about 200 microns or less than about 300 microns. It should

25 be understood that in one embodiment, the rib 1146 may be integrally formed with the cartridge or it may be attached or coupled to the cartridge after the cartridge is formed.

An analyte detecting member may occupy the opening 1148, form the underside of the

opening 1148, or some combination of the two. The analyte detecting member may be formed, configured, or shaped to receive fluid being spread off of the rib 1146. In some embodiments, there are no fluid bearing structures on the underside of the cartridge.

Figure 111 shows the underside of one embodiment of a cartridge 1152. For ease of illustration, the rib 1146 is made to appear thicker than it may actually be. In some embodiments, the rib may be about 100 μm thick. An thinned area 1154 is provided. The analyte detecting member may be formed to occupy a portion of the area 1154 corresponding to opening 1148 having rib 1146, formed to substantially fill the area 1154, formed to be placed against the surface 1154, or otherwise positioned to received fluid from openings 1146. In some embodiments, the electrodes forms the bottom surface of the chamber 1150 and can be viewed as being one "wall" of that chamber. The analyte detecting member may be visible though the opening 1148 when the cartridge 1152 is assembled (and the sterility barrier is punctured). A vent channel 1156 may be configured, in some embodiments, to draw excess fluid towards the vent 1158 via an opening 1160. In other embodiments, the vent channel 1156 is not present and excess blood or fluid simply fills the chamber 1150 or flows towards the narrowing 1162 (as seen in Figure 10).

Figure 112 shows an underside of a cartridge having two different fluid structures which may be used, singly or in combination. The embodiment on the right includes an area 1164 that results due to reduction in size of opening 1166. The sizing of the opening 1166 may be controlled depending on the amount of blood or fluid that the analyte detecting member needs to perform its analysis. In various embodiments, this may be less than about 1.0 μl , 0.9 μl , 0.8 μl , 0.7 μl , 0.6 μl , 0.5 μl , 0.4 μl , 0.3 μl , 0.2 μl , 0.1 μl , 0.05 μl , or 0.01 μl .

Figure 113 shows a top down view of one embodiment of a cartridge 1152 according to the present invention. In some configurations, a rib 1146 is provided in chamber 1150 to spread fluid to the analyte detecting members 1140, 1142, and 1144. In some embodiments, there are no fluid bearing structures on the underside of the cartridge. As a nonlimiting example, the analyte detecting member used in the present embodiment can provide its analysis using no more than about 1.0 μl , 0.9 μl , 0.8 μl , 0.7 μl , 0.6 μl , 0.5 μl , 0.4 μl , 0.3 μl , 0.2 μl , 0.1 μl , 0.05 μl , or 0.01 μl of fluid. In some embodiments, the amount of fluid used by all analyte members associated with each sample chamber 1150

can provide its analysis using no more than about 1.0 μ l, 0.9 μ l, 0.8 μ l, 0.7 μ l, 0.6 μ l, 0.5 μ l, 0.4 μ l, 0.3 μ l, 0.2 μ l, 0.1 μ l, 0.05 μ l, or 0.01 μ l of fluid. With the analyte detecting members such as those described in WO02/02796, the analyte detecting member used in the present embodiment can provide its analysis using no more than about 20 nanoliters, 5 15 nanoliters, 10 nanoliters, 5 nanoliters, or lower volumes. These detecting members such as members 1143 and 1148 may also be arranged in arrays 1145, 1147, or 1149. As a nonlimiting example, these analyte detecting members may be electrochemical based and use an ampiometric technique to measure an analyte. The analyte detecteing member may be printed on multiple surfaces, including but not limited to glass, ceramic, and 10 plastic. These analyte detecting members may include print hydrophilic channels, using hydrophilic layers with dimensions compatible with ver very small blood volume usage (50-100 micron heights).

Figure 114 is a close-up view of one embodiment of the cartridge having a plurality of analyte detecting members. A penetrating member 1168 is shown in this 15 view. In one embodiment, the penetrating member 1168 may start in this position, in the chamber 1150 prior to lancing. The penetrating member 1168 may also return to this position after lancing. In still further embodiments, the penetrating member 1168 may be advanced at a non-lancing speed to the position shown in Figure 114, stop, and then be actuated at lancing speeds to penetrate tissue. The sample chamber 1150 may, in one 20 embodiment, have only two analyte detecting members 1142 and 1144. In other embodiments, other analyte detecting members 1140, 1148, or 1143 (all shown in phantom) may be included.

Figure 115 shows one embodiment of an underside to cartridge 1152. In this embodiment, the analyte detecting members 1140, 1142, 1143, 1144, and 1148 are shown 25 as they would be positioned in area 1154. Leads or connectors 1108 may be coupled to the analyte detecting members. It should be understood that any of the analyte detecting members disclosed herein or known in the art may adapted for use with the present invention.

Referring now to Figures 116 and 117, a still further embodiment of the present 30 invention will now be described. In this embodiment of the cartridge, multiple fluid spreaders 1170 and 1172 are included for urging fluid into the various openings 1174, 1176, and 1178. In this embodiment, the spreaders may be integrally formed with the

cartridge. The analyte detecting members 1180 and 1182 in this embodiment are oriented perpendicularly to the openings 1174, 1176, and 1178.

Referring now to Figures 118 and 119, shows a variety of configurations of cavities and openings for use with a cartridge according to the present invention. These configurations may be used singly or in combination on a cartridge. The cavities 1116 5 may have vent openings 1184 in locations as shown in Figure 118. Some embodiments may have a chamber 1150 with an extended configuration as seen in the embodiment associated with position #4. In still further embodiments, the opening 1186 is not included and the only way to bring fluid to the underside is through one of the openings 10 1184, which may be at any of the locations shown for the cavity 1116. In still further embodiments, the analyte detecting member may be placed directly in the cavity 1116 without reliance on using a opening such as 1184 or 1186 to direct fluid to it. The analyte detecting member may be located anywhere in the cavity 1116 (on the side surfaces, bottom surfaces, etc...).

15 Figure 119 shows the underside configurations with numerals for each corresponding positions shown in Figure 118. In the configuration association with position #3, the opening 1186 connects directly to the open area 1188 which would correspond to the location of an analyte detecting member.

Referring now to Figure 120, a still further embodiment of the present invention 20 will now be described. This embodiment has a spreading element 1190 which, along with at least one analyte detecting member underneath the element 1190, forms the bottom wall of the chamber 1150. As a nonlimiting example, the element 1190 may have a mesh, a weaver, or "chainmail" type configuration. As seen in the Figure 120, the penetrating member 1168 may have a start position in the chamber 1150. The spreading 25 element 1190 may be made of a variety of materials, including but not limited to, a nitrocellulose polymer, cellulose nitrate, hydrophobic porous versions of Nylon, polysulfone, and polycarbonates. These elements 1190 may be membranes in some embodiments and can often be cast from a solution directly on the top of the sensing region. They may be configured morphologically in such a way as to wick blood exuding 30 from the lancing site and direct the flow of the whole blood or the plasma content on to a sensor. The propensity control and surface treatment may be varied to control the speed of flow (lateral or in through direction) or the rate of lateral spreading. Also they may be tailored to filter out particulates such as red blood cells. Additionally, the element 1190

may be a polymer mixed in with the detection chemistry or other material mixed in with detection chemistry. The element 1190 may occupy the entire area over the analyte detecting member, a portion, some geometric shape (round, rectangular, square, shapes with openings, figure eights, crisscrossed, gridded, etc...), or any combination of one or more of these configurations.

Referring now to Figures 121 and 122, a still further embodiment of a cartridge according to the present invention will now be described. The cartridge 1200 of Figure 121 includes a plurality of notches 1202 formed in an opening 1204 in the cartridge. These notches 1202 may be used for a variety of purpose, including but not limited to, 10 positioning of the cartridge 1200 in a lancing apparatus or for rotation purposes to change position of cavities 1116 aligned with a penetrating member launching device. The hub (not shown) which would mate with the opening 1204 may be rotating device that will be used to control which cavity 1116 and penetrating member is positioned for engagement with the launcher.

15 In one embodiment, the cartridge 1200 may include front bearing areas 1208 for guiding a penetrating member and rear bearing areas 1210. The rear bearing areas 1210 may be a length sufficient so that the penetrating member may create a wound in the target tissue without losing contact or guidance from the rear bearing area 1210. This provides for more control of the cutting path taken by the penetrating member. The 20 cavity provides sufficient open space for a penetrating member gripper to accommodate the throw distance used by the gripper to advance the penetrating member to contact tissue. In some embodiments, a middle guide bearing 1212 may be used. In such an embodiment, the gripper would grip a rear portion of the penetrating member, with both bearings remaining in "front" of the gripper, and the throw area of cavity 1116 moved 25 towards at least the rear half (in one embodiment) of the cartridge as indicated by arrow 1213 in Figure 123. As a nonlimiting example, the throw distance may be adjusted as desired to take up more than $\frac{1}{2}$ of cavity 1116, less than $\frac{1}{3}$, or less than $\frac{1}{4}$ of the cavity. A narrowed portion 1218 may be included to hold the penetrating members when the penetrating members are not being actuated.

30 As seen in Figure 122, the portion 1220 on the cartridge 1200 may be open or pressed to close the top surface of the front bearing (while still having an opening allowing the penetrating member to pass). The rear of cavity 1116 may be narrowed to

hold the penetrating member in place. Portions 1222 may also be used to deal with flash associated with the manufacturing process.

Referring now to Figures 124 and 125, embodiments of the present invention may comprise kits containing any of the penetrating member actuators 1230 disclosed herein.

- 5 The kit may further include instructions for use IFU setting forth any of the methods described above. Optionally, the kit may further comprise a cartridge containing a plurality of penetrating members. The cartridge 1232 may be of any of the embodiments disclosed herein (with or without penetrating members). Usually, the kit components will be packaged together in a pouch P or other conventional medical device packaging, such as but not limited to a box, tray, tube, or the like. In many embodiments, the cartridge will be disposable. The cartridge 1232 may itself be contained in a separate pouch or container and then inserted into the container P. In some embodiments, the IFU may be printed on the container P. In a nonlimiting example, the container P may only contain an actuator 1230, without the cartridge 1232.
- 10 Referring now to Figure 125, embodiments of the present invention may include kits that only include a cartridge 1232. IFU may also be included. In some embodiments, a plurality of cartridges 1232 (shown in phantom) may be included. Any of the elements in these figures or other elements described in this application may be placed in the container P, singly or in any combination.
- 15 A typical analyte detecting member has a optimum range of sensitivities. Figure 126 plots the sensitivity of a typical glucose sensor over concentration of glucose in the sample fluid. As seen in Figure 126, the glucose sensor is only accurate for detecting glucose levels over a limited range. Most sensor have their optimum sensitivity around about 3 mM (milimolar or micro moles per mL or 3 mmol per Litre). For high glucose levels or hyperglycemic ranges, the sensor is less accurate. For low glucose levels or hypoglycemic ranges, the sensor is less accurate as well. The sensor range can be shifted to cover higher glucose levels or lower glucose levels, but this is an inadequate solution as it sacrifices even more accuracy in the glucose range being shifted away from. Inaccuracies in glucose readings at the low sensitivity ranges can result in serious complications such as patients over-injecting the amount of insulin into their bodies.
- 20
- 25
- 30

"Nanoscopic" or "nano" is meant to include elements of widths or diameters of less than about 1 μm .

As used herein, a "nanowire" is an elongated nanoscale semiconductor which, at any point along its length, has at least one cross-sectional dimension and, in some 5 embodiments, two orthogonal cross-sectional dimensions less than 500 nanometers, preferably less than 200 nanometers, more preferably less than 150 nanometers, still more preferably less than 100 nanometers, even more preferably less than 70, still more preferably less than 50 nanometers, even more preferably less than 20 nanometers, still more preferably less than 10 nanometers, and even less than 5 nanometers. In other 10 embodiments, the cross-sectional dimension can be less than 2 nanometers or 1 nanometer. In one set of embodiments the nanowire has at least one cross-sectional dimension ranging from 0.5 nanometers to 200 nanometers. Where nanowires are described having a core and an outer region, the above dimensions relate to those of the core.

15 Referring now to Figure 127, one embodiment of the present invention will now be described. Figure 127 shows graphs of the sensitivities of multiple glucose analyte detecting members 1222, 1224, 1226, and 1228. As can be seen, the sensitivities of each analyte detecting member is optimized for different analyte concentrations. These areas of optimal sensitivity may be staggered. In glucose monitoring, this is particularly useful 20 as this configuration allows different sensitivities to be allocated to increase the range of coverage over that of a single conventional analyte detecting member. An array of analyte detecting members with non-identical sensitivity ranges enhances accuracy since the sensitivities may now cover an expanded range of concentrations. Accordingly, in one embodiment of the present invention, a plurality of analyte detecting members having 25 different sensitivities is used on the same body fluid sample.

Even an embodiment having only two of the analyte detecting members with different sensitivity ranges as shown in Figure 128 will improve analyte detecting member performance. Optionally in other embodiments, groups of analyte detecting members may be used wherein all the analyte detecting members in one group have the 30 same sensitivity range, but analyte detecting members in different groups have different ranges. This provides redundancy and statistical advantage as measurements over one range can be compared with another analyte detecting member in the same group measuring glucose in that same concentration range.

Referring now to Figure 129, an array 1242 of analyte detecting members such as those described in WO02/02796 may be used in a cartridge 1229 having a plurality of lancets or penetrating members 1240 and used with a driver 1236. For ease of illustration, only one of the plurality of penetrating members 1240 is shown. The array 5 1242 of analyte detecting members may be arranged near the lancet exit 1230 so that body fluid expressed from the patient may easily reach the array. The array 1242 may be located on the bottom surface of the module 1229, on the side surfaces, on the top surface, attached to a separate layer of material that is then attached to the module 1229, or some combination of any of these possibilities. The array 20 may be used with 10 microfluidic channels or tubes to guide body fluid to the analyte detecting members. The array 1242 may have a variety of configurations useful for maximizing accuracy of glucose monitoring. For example, array 1242 may have a circular configuration, a rectangular configuration (NxM, where N and M are integers), a triangular configuration, concentric configuration, or other design. Suitable designs for the sample module may be 15 found in commonly assigned, copending U.S. Provisional Patent Application Ser. No. 60/422,988 (Attorney Docket No. 38187-2601) filed November 1, 2002; in commonly assigned, copending U.S. Provisional Patent Application Ser. No. 60/424,429 (Attorney Docket No. 38187-2602) filed November 6, 2002; and in commonly assigned, copending U.S. Provisional Patent Application Ser. No. 60/428,084 (Attorney Docket No. 38187- 20 2604) filed November 20, 2002.

To enable the usage of multiple analyte detecting members in an everyday environment for glucose monitoring, it is desirable that the volumes of body fluid used for each analyte detecting member be reduced from conventional levels. From a practical standpoint, the amount of spontaneous blood from each lancet wound on the patient is 25 limited. Drawing too much blood would be impractical for the patient and may limit the number of samples a patient can or is willing to conduct in one day. Accordingly, the less blood or body fluid required for each analyte detecting member, the more analyte detecting members one can use on the blood or body fluid sample available through current lancing techniques. By way of example and not limitation, each glucose analyte 30 detecting member in one embodiment of the array of analyte detecting members may use blood volume of less than about 500 nanoliters. In other embodiments, each analyte detecting member uses less than about 300 nanoliters. In still other embodiments, each analyte detecting member uses less than about 50 nanoliters, less than about 30 nanoliters,

less than about 10 nanoliters, less than about 5 nanoliters, and less than about 1 nanoliters. In one embodiment of the present invention, sensors using nanowires such as those available from Nanosys, Inc. of Palo Alto California may be used to design small scale glucose or other analyte detecting members using low volumes as discussed above. In 5 one embodiment, these nanowires may be in the size of 100 nanometers by 20 nanometers. These nanowires may be made into a sensor design with electronics to monitor glucose and may be designed into a sensor of about 1 micrometer by 1 micrometer with between about 1-10 nanoliters blood requirement. In one embodiment, the nanowires may be used as electrodes with materials useful for glucose monitoring 10 immobilized on the nanowire. An array of 1238 of these analyte detecting member 1140 coupled to lead wires is shown in Figure 130. Figures 131 and 132 show other array configurations suitable for the present invention.

The nanowires used in the present invention may be fabricated using various techniques. For example, SiNWs (elongated nanoscale semiconductors) may be 15 synthesized using laser assisted catalytic growth (LCG). As shown in Figures 133A and 133B, laser vaporization of a composite target that is composed of a desired material (e.g. InP) and a catalytic material (e.g. Au) creates a hot, dense vapor which quickly condenses into liquid nanoclusters through collision with the buffer gas. Growth begins when the liquid nanoclusters become supersaturated with the desired phase and continues as long as 20 the reactant is available. Growth terminates when the nanowires pass out of the hot reaction zone or when the temperature is turned down. Au is generally used as catalyst for growing a wide range of elongated nanoscale semiconductors. However, the catalyst is not limited to Au only. A wide rage of materials such as (Ag, Cu, Zn, Cd, Fe, Ni, Co . . .) can be used as the catalyst. Generally, any metal that can form an alloy with the desired 25 semiconductor material, but doesn't form more stable compound than with the elements of the desired semiconductor can be used as the catalyst. The buffer gas can be Ar, N₂, and others inert gases. Sometimes, a mixture of H₂ and buffer gas is used to avoid undesired oxidation by residue oxygen. Reactive gas can also be introduced when desired (e.g. ammonia for GaN). The key point of this process is laser ablation generates liquid 30 nanoclusters that subsequently define the size and direct the growth direction of the crystalline nanowires. The diameters of the resulting nanowires are determined by the size of the catalyst cluster, which in turn can be varied by controlling the growth conditions (e.g. background pressure, temperature, flow rate . . .). For example, lower

pressure generally produces nanowires with smaller diameters. Using uniform diameter catalytic clusters can do further diameter control. Chemical vapor deposition also can be used to form nanotubes in arrays in the presence of directing electric fields, optionally in combination with self-assembled monolayer patterns.

Referring now to Figure 134, an array of sensors using nanowires will now be described. The nanowire sensor may comprise of a single molecule of doped silicon 100. The doped silicon is shaped as a tube, and the doping can be n-doped or p-doped. Either way, the doped silicon nanowire forms a high resistance semiconductor material across which a voltage may be applied. The exterior surface and the interior surface of the tube will have an oxide formed thereon and the surface of the tube can act as the gate 102 of an FET device and the electrical contacts at either end of the tube allow the tube ends to acts as the drain 106 and the source 108. In the depicted embodiment the device is symmetric and either end of the device may be considered the drain or the source. Figure 9 shows that the nanowire device is disposed upon and electrically connected to two conductor elements 104.

Figure 134 illustrates an example of a chemical/or ligand-gated Field Effects Transistor (FET). FETs are well known in the art of electronics. Briefly, a FET is a 3-terminal device in which a conductor between 2 electrodes, one connected to the drain and one connected to the source, depends on the availability of charge carriers in a channel between the source and drain. FETs are described in more detail in *The Art of Electronics*, Second Edition by Paul Horowitz and Winfield Hill, Cambridge University Press, 1989, pp. 113-174, the entire contents of which is hereby incorporated by reference. This availability of charge carriers is controlled by a voltage applied to a third "control electrode" also know as the gate electrode. The conduction in the channel is controlled by a voltage applied to the gate electrode, which produces an electric field across the channel. The device of Figure 134 may be considered a chemical or ligand-FET because the chemical or ligand provides the voltage at the gate, which produced the electric field, which changes the conductivity of the channel. This change in conductivity in the channel affects the flow of current through the channel. For this reason, a FET is often referred to as a transconductant device in which a voltage on the gate controls the current through the channel through the source and the drain. The gate of a FET is insulated from the conduction channel, for example, using a semi conductor junction such as in a junction FET (JFET) or using an oxide insulator such as in a metal oxide

semiconductor FET (MOSFET). Thus, in Figures A and B, the SiO₂ exterior surface of the nanowire sensor may serve as the gate insulation for the gate.

In application, the nanowire device illustrated in Figure 134 provides an FET device that may be contacted with a sample or disposed within the path of a sample flow.

- 5 Elements of interest within the sample can contact the surface of the nanowire device and, under certain conditions, bind or otherwise adhere to the surface. In one embodiment, the sensors 102 may each have a different sensitivity range, so as to enhance the overall accuracy of the array 107.

Referring now to Figure 135, the exterior surface of the device may have reaction entities, e.g., binding partners that are specific for a moiety of interest. The binding partners will attract the moieties or bind to the moieties so that moieties of interest within the sample will adhere and bind to the exterior surface of the nanowire device. An example of this is shown in Figure 135 where there is depicted a moiety of interest 120 (not drawn to scale) being bound to the surface of the nanowire device. With reference to Figure 135, that as the moieties build up, a depletion region 122 is created within the nanowire device that limits the current passing through the wire. The depletion region can be depleted of holes or electrons, depending upon the type of channel. The moiety has a charge that can lead to a voltage difference across the gate/drain junction.

The present invention may include, in one aspect, an integrated system, comprising a nanowire detector, a reader and a computer controlled response system. In this example, the nanowire detects a change in the equilibrium of an analyte in the sample, feeding a signal to the computer controlled response system causing it to withhold or release a chemical or drug. Such systems can be made capable of monitoring one, or a plurality of physiological characteristics individually or simultaneously. Such physiological characteristics can include, for example, oxygen concentration, carbon dioxide concentration, glucose level, concentration of a particular drug, concentration of a particular drug by-product, or the like. Integrated physiological devices can be constructed to carry out a function depending upon a condition sensed by a sensor of the invention. For example, a nanowire sensor of the invention can sense glucose level and, based upon the determined glucose level can cause the release of insulin into a subject through an appropriate controller mechanism.

As described above, the nanowires may be used with potentiometric techniques to monitor analyte levels. Potentiometric techniques monitor potential changes between a

working electrode and a reference electrode in response to charged ion species generated from enzyme reactions on the working electrode. Potentiometric biosensors make use of ion-selective electrodes in order to transduce the biological reaction into an electrical signal. In the simplest terms this consists of an immobilized enzyme membrane surrounding the probe from a pH-meter, where the catalyzed reaction generates or absorbs hydrogen ions. The reaction occurring next to the thin sensing glass membrane causes a change in pH, which may be read directly from the pH-meter's display. Typical of the use of such electrodes is that the electrical potential is determined at very high impedance allowing effectively zero current flow and causing no interference with the reaction.

A microelectronic potentiometric biosensor, the Field Effect Transistor (FET) biosensor, may be used for analyte sensing. In this design, a receptor or molecular recognition species is coated on a transistor gate. When a ligand binds with the receptor, the gate electrode potential shifts, thereby controlling the current flowing through the FET. This current is detected by a circuit, which converts it to an observed ligand concentration. The glucose sensor may be similar in construction to the oxygen sensor. One difference is that a hydrophilic membrane with immobilized glucose oxidase (i.e., GOD) is used instead of the hydrophobic oxygen membrane. In the presence of glucose oxidase, the following reaction occurs:

20



In this case, glucose concentration can be determined by polarizing the working electrode either anodically or cathodically by approximately 700 mV, to measure the rate 25 of hydrogen peroxide oxidation or oxygen reduction.

A potentiometric sensor produces an electrical voltage that varies with the species of interest. Ionic species, such as hydrogen ion (H^{+}), sodium (Na^{+}), potassium (K^{+}), ionized calcium (Ca^{++}) and chloride (Cl^{-}), are commonly measured by ion-selective electrodes, a typical class of potentiometric sensors.

30 The commonly used CO_2 sensor, sometimes known as the Severinghaus electrode, also is a potentiometric sensor (and is, in fact, essentially a modified pH sensor). Typically, it consists of a pH electrode and a reference electrode, with both covered by a hydrophobic, gas-permeable/liquid-impermeable membrane such as

silicone. A thin layer of weakly buffered internal electrolyte, e.g., 0.001 M NaHCO₃, is located between the hydrophobic membrane and the pH sensing membrane. Carbon dioxide in the sample eventually reaches equilibrium with the internal electrolyte, and it produces a pH shift according to the following equation:

5



- The pH electrode then measures the resulting pH shift. Therefore, a direct relationship exists between a sample's CO₂ partial pressure (pCO₂) and its pH.
- 10 The accuracy of measurement obtained with any of the above-described sensors can be adversely affected by drift, particularly after exposure to biological fluids such as whole blood. Frequent calibration may be required. This is particularly true for gases such as pO₂ and pCO₂, because any change in the gas transport properties of the membrane can affect the sensor output. With multiple sensors in an array configuration,
- 15 some may be dedicated for calibration purpose. Additionally, the use of many sensors over the same sensitivity range provides statistical advantage in that error from one sensor may be ignored while the other continue to generate accurate readings.

Referring now to Figure 136, another embodiment of sensor is described. Figure 136 shows a schematic diagram of the section across the width of an ENFET. The actual dimensions of the active area may be about 500 μm long by 50 μm wide by 300 μm thick, though it should be understood that the device may be constructed to even smaller dimensions. The main body of the biosensor is a p-type silicon chip with two n-type silicon areas; the negative source and the positive drain. The chip is insulated by a thin layer (0.1 mm thick) of silica (SiO₂) which forms the gate of the FET. Above this gate is an equally thin layer of H⁺-sensitive material (e.g. tantalum oxide), a protective ion selective membrane, the biocatalyst and the analyte solution, which is separated from sensitive parts of the FET by an inert encapsulating polyimide photopolymer. When a potential is applied between the electrodes, a current flows through the FET dependent upon the positive potential detected at the ion-selective gate and its consequent attraction of electrons into the depletion layer. This current (I) is compared with that from a similar, but non-catalytic ISFET immersed in the same solution. (Note that the electric current is, by convention, in the opposite direction to the flow of electrons). The sensitive materials used may be replaced with those specific for glucose monitoring.

- Glucose monitoring material may be immobilized on the nanowire using various techniques. For example, although various conducting polymers may be used for immobilization of enzymes and other bioactive substances, polypyrrole (PPy) has gained interest for the entrapment of protein molecules because of its low oxidation potential.
- 5 This characteristic enables the growth of film from aqueous solutions, which are compatible with most biological systems. This approach is usually based on entrapment of an enzyme into the structure of polypyrrole film by potentiostatic or galvanostatic polymerisation in the presence of the enzyme in a monomer solution, which often contains supporting electrolyte. The immobilisation of glucose oxidase (GOD) into
- 10 polypyrrole films is one of the widely investigated polypyrrole-based biosensor for selective measurement of glucose. A potentiometric glucose biosensor may be fabricated via the immobilization of GOD with PPy film on an inert Pt electrode in aqueous monomer solutions without the addition of supporting electrolyte. In particular, the use of ultra-thin PPy-GOD films for more rapid and sensitive potentiometric biosensing of
- 15 glucose has been demonstrated. (Electrochemical News, Spring 1999 Vol 4. No.2, Potentiometric Biosensing of Glucose with Ultra-thin Polypyrrole-Glucose Oxidase Films, Sam B. Adelaju and Alex N. Moline).

The deposition of individual and intact preformed supramolecular assemblies of biomolecules onto a suitable solid substrate can result in assemblies that serve as self-contained modules for the fabrication of molecular sensors and devices. Laser-assisted deposition (LAD) is a unique tool for the formation of thin films of materials and has been used successfully for the fabrication of nanostructures. The technique offers the possibility of arranging preformed assemblies in well-defined architectures by physically lifting and depositing molecular assemblies onto solid surfaces. The LAD technique has been used to deposit glucose oxidase in sodium dodecyl sulphate, riboflavin in phospholipids and, more recently, photosensitive bacteriorhodopsin(bR) in a matrix of the lipid L--distearoyl phosphatidyl-choline. bR is a component of the purple membrane of the halophile Halobacterium halobium and functions as a light driven proton pump, with potential applications in photochromic, holographic, nonlinear optical and information processing devices. A monolayer of bR fabricated by self-assembly forms a bistable red/green switch that operates in 500 fs and stores data with 10,000 molecules per bit.

A process developed by A.C. Fou et al. may also be used for the fabrication of layer-by-layer nano-architectures films of polypyrrole (PPY) via in-situ self-assembly.

Among redox active enzymes, the electrochemical behavior of glucose oxidase (GOD) was actively investigated, due to its practical applications in manufacturing biological sensors. The immobilisation of GOD on a conductive polymer (PPY, polyaniline, etc.) allows the construction of glucose responsive biosensors, for which the immobilisation of 5 single or clustered GOD molecules represents a crucial and important step.

Deposition techniques may also be used to deposit glucose oxidase on the sensor. Referring to Figure 137, a vapor deposition technique known as matrix assisted pulsed-laser evaporation (MAPLE) may be used to deposit materials on a nanowire, nanotube, other nanostructure, or a small electrode. The process may generate high quality 10 polymeric, organic, and biomaterial films on many types of substrates. The technique has been used to deposit a wide range of organic and inorganic polymers, biopolymers, and low to intermediate molecular weight organics as thin, uniform, and adherent coatings. These films are grown-with areas of a few square micrometers and in thicknesses ranging from about 5 nm to several micrometers over extended areas without degrading the 15 physicochemical properties of the deposited materials. Although the new process may be similar to conventional PLD-both are vacuum-deposition techniques and they share many of the same advantages over traditional thin-film fabrication techniques-the new process has additional capabilities for depositing polymer thin films. First, the organic material arrives at the substrate surface free of solvating molecules, which eliminates solvent 20 wetting and allows better control of coating placement. Second, the growth of multi-layer structures of different compounds occurs without mixing at the layer interfaces, instead of the thin film of mixed materials that results from the solvent effects. And, unlike most traditional polymer or organic thin-film-fabrication techniques, MAPLE simultaneously 25 deposits contamination-free films with monolayer thickness control(independent of the total thickness);requires minimal amounts of material; and provides enhanced film adhesion to the substrate. It is also easily combined with masking techniques (contact and noncontact).

The MAPLE process uses a frozen matrix as the laser target. This matrix, which consists of a dilute solution of a polymer or organic material in a volatile solvent, may 30 absorb the laser pulse and allow the solute molecules to be gently desorbed from the target. At the molecular level, the technique is a photothermal process. Simply stated, the incident laser energy is absorbed by the bulk solvent molecules and converted into kinetic energy, which is then transferred to the embedded solute through collective collisions,

resulting in the desorption of large molecular weight species. By carefully optimizing deposition conditions, this process takes place without significant decomposition or damage of the coating material. As in PLD, the laser pulse generates a forward directed vapor cone containing the evaporated material. When a substrate is positioned directly in
5 this path, it is uniformly coated with the solute coating material while the volatile solvent molecules are removed by the chamber's vacuum pump. In principle, the process is similar to the chemical analytical technique called matrix assisted laser desorption-ionization mass spectrometry (MALDI-MS), a process developed for studying macromolecules to determine their molecular weight distributions. A significant
10 difference between the two techniques lies in the treatment of the evaporated material. In the MAPLE process, the material of interest is not deliberately ionized or decomposed, but it is collected as a coating on a substrate rather than being directed into a mass spectrometer for further analysis. A unique advantage of the emerging process is that it can be easily combined with noncontact shadow masks to limit the deposition to a
15 required area. This is useful for coating fragile substrates, such as polymer coatings on atomic force microscope cantilevers, and is less expensive and less time consuming than subsequent removal by patterning and etching. Patterns of polymer and organic materials with features on a 10- μm scale have been generated by MAPLE depositions through masks. This capability is important for the manufacture of sensor arrays and electronic
20 components, in which the desired coating area is measured in micrometers. Another advantage of the technique is that the polymer or organic material is deposited on a substrate free of bulk solvent. In contrast, deposition techniques such as aerosol, spin, ink-jet, and dip coating may use a solution of the material in a solvent to physically wet the surface of a substrate. Such techniques limit the surface choices to materials that the
25 solvent does not dissolve. The uneven and unpredictable wetting, distribution, and evaporation of the solvent molecules result in nonuniform coatings. As examples of coatings using this process, thin films of glucose oxidase, an enzyme used for glucose monitoring, have been deposited on the electrodes of miniature sensors. The resulting devices perform as well as those deposited by ink-jet techniques, with superior uniformity
30 and coverage.

It should be understood that different sensors detecting different ranges of glucose concentration, different analytes, or the like may be combined for use with each penetratring member. Non-potentiometric measurement techniques may also be used for

analyte detection. For example, direct electron transfer of glucose oxidase molecules adsorbed onto carbon nanotube powder microelectrode may be used to measure glucose levels. In all methods, nanoscopic wire growth can be carried out via chemical vapor deposition (CVD). In all of the embodiments of the invention, preferred nanoscopic wires may be nanotubes. Any method useful for depositing a glucose oxidase or other analyte detection material on a nanowire or nanotube may be used with the present invention. In some embodiments, these nanowires are integrated into lancets or other penetrating members which measure analyte levels. Expected variations or differences in the results are contemplated in accordance with the objects and practices of the present invention.

Figure 138 shows a still further embodiment where a cartridge 1300 for holding a single penetrating member is shown. A plastic or other overlay sheet is printed with a plurality of low volume analyte detecting members 1140 is attached to the cartridge 1300. Body fluid will be drawn into sample chamber 1302 where the member 1140 will detect the analytes in the fluid. It should be understood of course that other numbers of analyte detecting members may be attached to the sheet 1304 and is not limited to the embodiment shown in this Figure 138.

Figure 139 shows a top down view of one embodiment of a cartridge 1152 according to the present invention. A rib 1146 is provided in chamber 1150 to spread fluid to the analyte detecting members 1140, 1142, and 1143. In this embodiment, the rib 1146 may be spaced apart from the analyte detecting members 1140 and 1142, allowing fluid to flow between the structures. In other embodiments, the analyte detecting members may be flush against the rib 1146. In some embodiments, there are no fluid bearing structures on the underside of the cartridge. As a nonlimiting example, the analyte detecting member used in the present embodiment can provide its analysis using no more than about 1.0 μ l, 0.9 μ l, 0.8 μ l, 0.7 μ l, 0.6 μ l, 0.5 μ l, 0.4 μ l, 0.3 μ l, 0.2 μ l, 0.1 μ l, 0.05 μ l, or 0.01 μ l of fluid. In some embodiments, the amount of fluid used by all analyte members associated with each sample chamber 1150 can provide its analysis using no more than about 1.0 μ l, 0.9 μ l, 0.8 μ l, 0.7 μ l, 0.6 μ l, 0.5 μ l, 0.4 μ l, 0.3 μ l, 0.2 μ l, 0.1 μ l, 0.05 μ l, or 0.01 μ l of fluid.

Figure 140 is a close-up view of the embodiment of Figure 114. A penetrating member 1168 is shown in this view. In one embodiment, the penetrating member 1168

may start in this position, in the chamber 1150 prior to lancing. The penetrating member 1168 may also return to this position after lancing. In still further embodiments, the penetrating member 1168 may be advanced at a non-lancing speed to the position shown in Figure 114, stop, and then be actuated at lancing speeds to penetrate tissue.

5 Figure 141 shows an embodiment of an underside to cartridge 1152. In this embodiment, the analyte detecting members 1140, 1142, and 1143 are shown as they would be positioned in area 1154. Leads or connectors 1108 may be coupled to the analyte detecting members. It should be understood that any of the analyte detecting members disclosed herein or known in the art may be adapted for use with the present
10 invention.

Referring now to analyte detecting members in Figures 139-141, it should be understood that, although not limited to the following, in this embodiment, the analyte detecting members may be designed as follows. The analyte detecting member may be based on chrono-amperometry measurement technique using glucose oxidase (Gox) 15 enzyme and N,N,N',N'-Tetramethyl-p-phenylenediamine (TMPD), as electron transfer mediator. In one embodiment, the analyte detecting member is a screen-printed three-electrode system. The conducting layers may be made with a commercially available carbon paste. The reference and the counter electrodes 1142 and 1143 may be made of a commercial formulation of Ag/AgCl. Although not limited to the following, the working
20 electrode 1140 may be made from the same commercial carbon paste blended with Gox, the mediator, a buffer and a thinner. The device has optimized the composition of the working electrode material to lower the response time. A phosphate buffer may be used to mitigate pH sensitivity of the mediator.

Additionally, a hydrophilic membrane with a surfactant may be used that
25 stabilizes an otherwise sublimable mediator such as TMPD. This is, presumably, achieved due to low solubility of the mediator in the hydrophilic membrane.

In one embodiment, the device for reading glucose signal is a voltage source providing a constant oxidation potential of 130 mV between the working electrode and the reference electrode. The output signal is the current flow between the working electrode
30 and the counter electrode. The average of eleven successive current readings (measured over 110 milliseconds) after reaching a predetermined equilibrium point is read out. The glucose composition is calculated using one of two calibration lines depending upon the concentration range.

The substrate on which the electrode is formed may be a UV stabilized thick PVC film on which the electrodes, the insulating layer and the active materials may be deposited using screen-printing process. In some embodiments, this PVC layer may be about 750 μm thick. The sample-contacting region on the electrodes is covered with a 5 screen-printed hydrogel (~4 μm thick). For the sip-in sensors, the spacer film forms the sidewalls and defines the thickness of the sample region. This may be a double-sided PSA layer or a screen-printed UV curable adhesive. The cover may be a 127 μm polyester film coated with 8-15 μm hydrophilic coating on the sample-contact side.

Referring now to Figure 142, a cross-section of the analyte detecting members are 10 shown. In this embodiment, a substrate 1400 is provided. On top of this substrate, a carbon paste is provided to form conducting layers 1402 for a screen-printed three-electrode system. A spacer layer 1404 may also be provided. The reference and the counter electrodes 1142 and 1143 may be made of a formulation of Ag/AgCl. The analyte detecting member may be based on chrono-amperometry measurement technique 15 using glucose oxidase (Gox) enzyme and N,N,N',N'-Tetramethyl-p-phenylenediamine (TMPD), as electron transfer mediator. Although not limited to the following, the working electrode 1140 may optionally comprise of carbon paste blended with Gox, the mediator, a buffer and a thinner. A hydrophilic layer or membrane 1408 is provided on top of the electrodes. In some embodiments, only the working electrode 1140 has the 20 hydrophilic layer 1408.

Figure 143 shows that the layers in Figure 142 may be arranged in a manner as shown. Figure 143 is an exploded view of the various layers. The spacer 1404 may be shaped as shown, may be shaped to match the substrate 1400, or otherwise configured to allow the formation of the electrodes. The length and shape of the conductive layers 1402 25 may also be varied depending on where the electrodes are located and where the connection pads are for connection to a metering portion of the device. In one embodiment, the layers 1402 may extend to the inner diameter of the substrate 1400.

Referring now to Figure 144 through 146, one embodiment of a radial disc having 30 a plurality of analyte detecting members will be described. Figure 144 shows that the disc 1420 may include a plurality of electrodes of the types as described in Figure 142. Of course, it should be understood that other type of electrodes and testing techniques may also be adapted for use with the disc 1420.

As seen in Figure 145, a connector disc 1430 provides a plurality of connector pads 1432 to facilitate electrical connection with connectors on the metering portion of the device. Although not limited to the following, each connector pad 1432 may have a size of at least 1 mm² to facilitate sliding contact with the metering device. The disc 1430 has smaller pads 1434 for matching up with pads 1422 on the analyte detecting member disc 1420.

Referring now to Figure 146, it can be seen that the discs 1420 and 1430 can be combined together. In one embodiment as seen in Figure 147, the connector disc 1430 is located between a substrate such as, but not limited to, a disc 500 and the analyte detecting member disc 1430. Although no limited to the following, in some embodiments, the thickness of the connector disc may be less than approximately 50 µm. The dimensions of the connector disc 1430 in one embodiment has a 25 mm inner diameter and a 46 mm outer diameter. The dimensions for various pads 1432 and related structure are shown in Figure 148 for one embodiment of the present invention.

In another embodiment, another way for creating a contact between connector pads of the sensor-disc with the sliding contacts of the meter is to bring the connector pads directly on the disc 500. In this case, connector disc 1430 may become optional. In this embodiment, the connector lines as well as the connector pads may be printed directly on the disc 500 by screen-printing. Although not limited to the following, the layout for the screens for printing the connector lines and the connector pads on the disc 500 may be the same as the layout for the screens for printing the connector lines and the connector pads on the connector-disc 1430. For this printing procedure, a carrier (e.g., aluminium) having recesses for the discs 500 may be used. The value of the deep of the recess may be the same as the value of the thickness of the disc 500. Furthermore, the recesses in the carrier material may be constructed in such a way, that disc 500 will fix into the recess in a prescribed position. For performing a printing step directly on the disc 500, in this embodiment, there is little change to the disc 500. A very plane surface of the upper side (close to the sensor-disc) of the disc 500 may be used. In some embodiments, the rectangular recesses on the disc 500 are located at a position where the electrodes of the analyte detecting member disc 1420 may be positioned.

Figure 149 shows the combined discs 1420 and 1430 may include a center portion 1440 that is keyed and shaped to enable rotation of the disc. Gear teeth may be provided on the inner diameter surfaces of the center portion 1440.

Figure 150 shows that in some embodiments, the disc 1450 is solid without an opening in the center. As a nonlimiting example, a variety of indentations, gear teeth or other shapes or structures as mentioned in regards to Figure 52 may be formed on the disc and used to enable rotation and/or indexing of the disc. These structural formations may 5 be on the top, bottom, inner diameter, or outer periphery of the disc. Notches may also be used on the outer periphery and other surfaces. Although not limited to the following, any of the discs disclosed herein may be adapted for use with seals as shown herein such as but limited to a sealing layer 1106 to protect the analyte detecting members. Any of the analyte detecting member densities as disclosed herein may also be applicable to the discs 10 disclosed.

Figure 151 shows that varying numbers of analyte detecting members may be provided on each disc. In the embodiment of the Figure 151, the disc 1460 provides enough analyte detecting members for 25 analyte measurement tests. It should be understood that any number of analyte detecting member may be provided on a disc such 15 as but not limited to more than 17. Some may have no less than 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 analyte detecting members. Some may have different analyte detecting members for measuring different analytes. The disc 1460 may be adapted for use in a housing 1462 (shown in phantom) having a cut out 1464 that exposes only one, three-electrode analyte detecting member at a time. This allows the 20 others to remain protected prior to use. The disc 1460 will rotate to bring an unused analyte detecting member into position for use. In some embodiments, microfluidics and/or other methods as described herein may be used to draw fluid toward the analyte detecting members. Although not limited to the following, these microfluidics and other structures may be formed near the outer periphery of the disc.

25 Figures 152 and 153 show still further embodiments showing that analyte detecting members 1470 may be mounted on substrate of a variety of shapes including but not limited to cylindrical as shown. Other shapes such as but limited to square, wedges, half circles, pie wedges, triangular, wagon wheel, propeller, any combination of the above or other shapes may be used. Figure 152 shows the members 1470 mounted on 30 a side wall of cylinder 1472. Figure 153 shows that the members 1470 may be mounted on a face of a cylinder. The cylinder in figure 152 may be hollow. Other shapes such as but not limited to cones, spheres, cubes, columns, squares, rectangles, a concave or convex disc, combinations of these shapes, or the like may also be used.

While the invention has been described and illustrated with reference to certain particular embodiments thereof, those skilled in the art will appreciate that various adaptations, changes, modifications, substitutions, deletions, or additions of procedures and protocols may be made without departing from the spirit and scope of the invention.

- 5 For example, with any of the above embodiments, the location of the penetrating member drive device may be varied, relative to the penetrating members or the cartridge. With any of the above embodiments, the penetrating member tips may be uncovered during actuation (i.e. penetrating members do not pierce the penetrating member enclosure or protective foil during launch). With any of the above embodiments, the penetrating
- 10 members may be a bare penetrating member during launch. With any of the above embodiments, the penetrating members may be bare penetrating members prior to launch as this may allow for significantly tighter densities of penetrating members. In some embodiments, the penetrating members may be bent, curved, textured, shaped, or otherwise treated at a proximal end or area to facilitate handling by an actuator. The
- 15 penetrating member may be configured to have a notch or groove to facilitate coupling to a gripper. The notch or groove may be formed along an elongate portion of the penetrating member. With any of the above embodiments, the cavity may be on the bottom or the top of the cartridge, with the gripper on the other side. In some embodiments, analyte detecting members may be printed on the top, bottom, or side of
- 20 the cavities. The front end of the cartridge maybe in contact with a user during lancing. The same driver may be used for advancing and retraction of the penetrating member. The penetrating member may have a diameters and length suitable for obtaining the blood volumes described herein. The penetrating member driver may also be in substantially the same plane as the cartridge. The driver may use a through hole or other opening to engage a proximal end of a penetrating member to actuate the penetrating member along a path into and out of the tissue.
- 25

Any of the features described in this application or any reference disclosed herein may be adapted for use with any embodiment of the present invention. For example, the devices of the present invention may also be combined for use with injection penetrating members or needles as described in commonly assigned, copending U.S. Patent Application Ser. No. 10/127,395 (Attorney Docket No. 38187-2551) filed April 19, 2002. An analyte detecting member to detect the presence of foil may also be included in the lancing apparatus. For example, if a cavity has been used before, the foil or sterility

barrier will be punched. The analyte detecting member can detect if the cavity is fresh or not based on the status of the barrier. It should be understood that in optional embodiments, the sterility barrier may be designed to pierce a sterility barrier of thickness that does not dull a tip of the penetrating member. The lancing apparatus may 5 also use improved drive mechanisms. For example, a solenoid force generator may be improved to try to increase the amount of force the solenoid can generate for a given current. A solenoid for use with the present invention may have five coils and in the present embodiment the slug is roughly the size of two coils. One change is to increase the thickness of the outer metal shell or windings surround the coils. By increasing the 10 thickness, the flux will also be increased. The slug may be split; two smaller slugs may also be used and offset by $\frac{1}{2}$ of a coil pitch. This allows more slugs to be approaching a coil where it could be accelerated. This creates more events where a slug is approaching a coil, creating a more efficient system.

In another optional alternative embodiment, a gripper in the inner end of the 15 protective cavity may hold the penetrating member during shipment and after use, eliminating the feature of using the foil, protective end, or other part to retain the used penetrating member. Some other advantages of the disclosed embodiments and features of additional embodiments include: same mechanism for transferring the used penetrating members to a storage area; a high number of penetrating members such as but not limited 20 to 25, 50, 75, 100, 500, or more penetrating members may be put on a disk or cartridge; molded body about a lancet becomes unnecessary; manufacturing of multiple penetrating member devices is simplified through the use of cartridges; handling is possible of bare rods metal wires, without any additional structural features, to actuate them into tissue; maintaining extreme (better than 50 micron -lateral- and better than 20 micron vertical) 25 precision in guiding; and storage system for new and used penetrating members, with individual cavities/slots is provided. The housing of the lancing device may also be sized to be ergonomically pleasing. In one embodiment, the device has a width of about 56 mm, a length of about 105 mm and a thickness of about 15 mm. Additionally, some 30 embodiments of the present invention may be used with non-electrical force generators or drive mechanism. For example, the punch device and methods for releasing the penetrating members from sterile enclosures could be adapted for use with spring based launchers. The gripper using a frictional coupling may also be adapted for use with other drive technologies.

Still further optional features may be included with the present invention. For example, with any of the above embodiments, the location of the penetrating member drive device may be varied, relative to the penetrating members or the cartridge. With any of the above embodiments, the penetrating member tips may be uncovered during actuation (i.e. penetrating members do not pierce the penetrating member enclosure or protective foil during launch). The penetrating members may be a bare penetrating member during launch. The same driver may be used for advancing and retraction of the penetrating member. Different analyte detecting members detecting different ranges of glucose concentration, different analytes, or the like may be combined for use with each penetrating member. Non-potentiometric measurement techniques may also be used for analyte detection. For example, direct electron transfer of glucose oxidase molecules adsorbed onto carbon nanotube powder microelectrode may be used to measure glucose levels. In some embodiments, the analyte detecting members may be formed to flush with the cartridge so that a "well" is not formed. In some other embodiments, the analyte detecting members may be formed to be substantially flush (within 200 microns or 100 microns) with the cartridge surfaces. In all methods, nanoscopic wire growth can be carried out via chemical vapor deposition (CVD) or other vapor deposition. In all of the embodiments of the invention, nanoscopic wires may be nanotubes. Any method useful for depositing a glucose oxidase or other analyte detection material on a nanowire or nanotube may be used with the present invention. Additionally, for some embodiments, any of the cartridge shown above may be configured without any of the penetrating members, so that the cartridge is simply an analyte detecting device. Still further, the indexing of the cartridge may be such that adjacent cavities may not necessarily be used serially or sequentially. As a nonlimiting example, every second cavity may be used sequentially, which means that the cartridge will go through two rotations before every or substantially all of the cavities are used. As another nonlimiting example, a cavity that is 3 cavities away, 4 cavities away, or N cavities away may be the next one used. This may allow for greater separation between cavities containing penetrating members that were just used and a fresh penetrating member to be used next. It should be understood that nanowires may be used with any embodiment of the cartridges described herein. The size and diameters of the radial cartridges described herein may also vary and are not limited to the sizes shown herein.

This application cross-references commonly assigned copending U.S. Patent Applications Ser. No. 10/323,622 (Attorney Docket No. 38187-2606) filed December 18, 2002; commonly assigned copending U.S. Patent Applications Ser. No. 10/323/623 (Attorney Docket No. 38187-2607) filed December 18, 2002; and commonly assigned 5 copending U.S. Patent Applications Ser. No. _____ (Attorney Docket No. 38187-2609) filed December 18, 2002. The present application is related to commonly assigned, co-pending U.S. Patent Application Ser. Nos. US: 10/335,215; 10/335,258; 10/335,099; 10/335,219; 10/335,052; 10/335,073; 10/335,220; 10/335,252; 10/335,218; 10/335,211; 10/335,257; 10/335,217; 10/335,212; 10/335,241; 10/335,183; 10/335,082; 10/335,240; 10 10/335,259; 10/335,182; (Attorney Docket Nos. 38187-2633 through 38187-2652), filed December 31, 2002. All applications listed above are fully incorporated herein by reference for all purposes. The publications discussed or cited herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present invention is not entitled to antedate such 15 publication by virtue of prior invention. Further, the dates of publication provided may be different from the actual publication dates which may need to be independently confirmed. All publications mentioned herein are incorporated herein by reference to disclose and describe the structures and/or methods in connection with which the publications are cited.

20 Expected variations or differences in the results are contemplated in accordance with the objects and practices of the present invention. It is intended, therefore, that the invention be defined by the scope of the claims which follow and that such claims be interpreted as broadly as is reasonable.

WHAT IS CLAIMED IS:

1. A device for use with a metering device for measuring analyte levels, said device comprising:
 - 3 a cartridge;
 - 4 a plurality of analyte detecting members mounted on said cartridge.
1. 2. The device of claim 1 wherein said cartridge does not include any penetrating members.
1. 3. The device of claim 1 wherein said cartridge has a radial disc shape.
1. 4. The device of claim 1 wherein said cartridge is sized to fit within said metering device.
1. 5. The device of claim 1 wherein said analyte detecting members wherein only a working electrode is covered with a glucose oxidase.
1. 6. The device of claim 1 wherein said analyte detecting members include working and counter electrodes formed from one of the following: Ag or Ag/Cl.
1. 7. The device of claim 1 wherein said analyte detecting members have different sensitivity ranges enhancing the overall range of sensitivity of an array of such members when used on a single fluid sample.
1. 8. The device of claim 1 wherein said analyte detecting members can provide their analysis requiring no more than one of the following volumes: 300, 200, 100, 60, 50, 30, 20, 15, 10, and 5 nanoliters.
1. 9. The device of claim 1 wherein said analyte detecting member comprises a working electrode, a reference electrode, and counter electrode, wherein only the working electrode is covered with a redox mediator.
1. 10. The device of claim 1 said analyte detecting members use an amperometric measurement technique.

- 1 11. The device of claim 1 further comprising a mesh configured fluid
2 spreader positioned over said analyte detecting member.
- 1 12. The device of claim 1 further comprising a hydrophilic membrane
2 positioned over said analyte detecting member. 4.53 cubic centimeters
- 1 13. The device of claim 1 wherein the cartridge has a higher density of
2 analyte detecting members than 4.53 cubic centimeters divided by 17 per single analyte
3 detecting member..
- 1 14. The device of claim 1 wherein the cartridge has a higher density of
2 analyte detecting members than 4.53 cubic centimeters divided by 20 per single analyte
3 detecting member.
- 1 15. The device of claim 1 wherein the cartridge has a higher density of
2 analyte detecting members than 4.53 cubic centimeters divided by 25 per single analyte
3 detecting member.
- 1 16. The device of claim 1 wherein the cartridge has a higher density of
2 analyte detecting members than 4.53 cubic centimeters divided by 50 per single analyte
3 detecting member.
- 1 17. A device for use with a body fluid sampling device for extracting
2 bodily fluid from an anatomical feature, said device comprising:
3 a cartridge having a plurality of sample chambers;
4 a plurality of analyte detecting members;
5 wherein at least one of said analyte detecting members forms a portion of
6 one wall of one of said plurality of sample chambers.
- 1 18. The device of claim 17 wherein said cartridge comprises a
2 connector disc and an analyte detecting member disc.
- 1 19. A device for use with a body fluid sampling device for extracting
2 bodily fluid from an anatomical feature, said device comprising:
3 a cartridge having a plurality of sample chambers;

4 a plurality of penetrating members each at least partially contained in said
5 cavities of the single cartridge wherein the penetrating members are slidably movable to
6 extend outward from openings on said cartridge to penetrate tissue;
7 a plurality of analyte detecting members;
8 wherein said chamber is positioned substantially adjacent an outer
9 periphery of said cartridge;
10 at least one opening in one of said sample chambers leading fluid along a
11 fluid path towards one of said analyte detecting members.

1 20. The device of claim 19 wherein said fluid path contains a channel
2 sized to hold no more than 1 microliter.

1 21. A method for determining a concentration of an analyte in body
2 fluid, comprising:
3 collecting a sample of body fluid of about 500 nL or less;
4 covering an electrochemical sensor with at least a portion of the sample;
5 determining the concentration of the analyte in the sample using a
6 potentiometric technique.

1 22. A device comprising:
2 a plurality of analyte detecting members defining an array;
3 wherein at least two of said members have different sensitivity ranges
4 enhancing the overall range of sensitivity of the array when used on a sample fluid.

1 23. A device comprising:
2 a single cartridge having a plurality of cavities;
3 a plurality of analyte detecting members defining an analyte array;
4 wherein at least two of said sensors have different sensitivity ranges
5 enhancing the overall range of sensitivitiv of the array when used on a sample fluid;
6 wherein said plurality of cavities each has one analyte array.

1 24. A system comprising:
2 an electric penetrating member driver;
3 a single cartridge having a plurality of cavities;
4 a plurality of penetrating members housed in said cavities and individually
5 movable by said driver to penetrate tissue;

6 a plurality of analyte detecting members defining an analyte array;
7 wherein at least two of said sensors have different sensitivity ranges
8 enhancing the overall range of sensitivity of the array when used on a sample fluid;
9 wherein said plurality of cavities each has one analyte array.

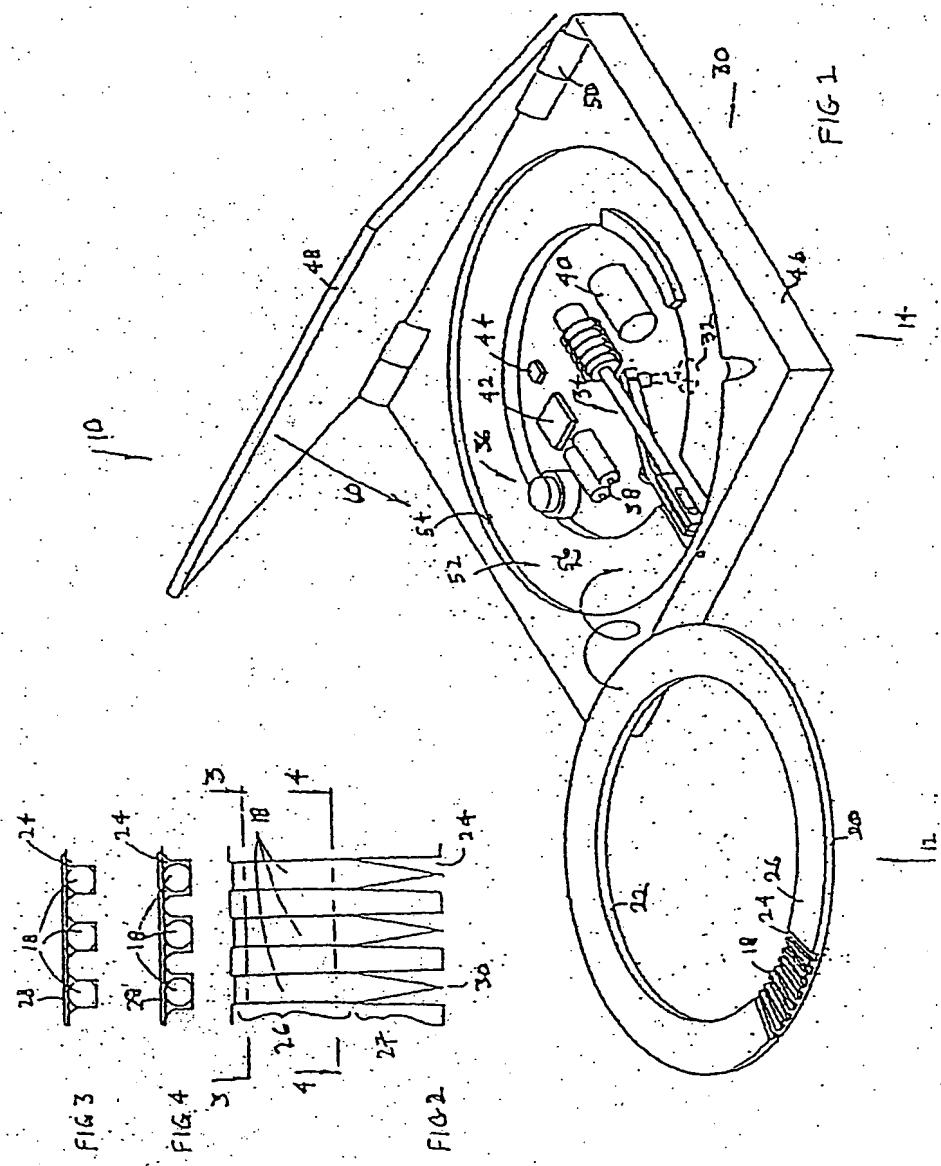


FIG 6A

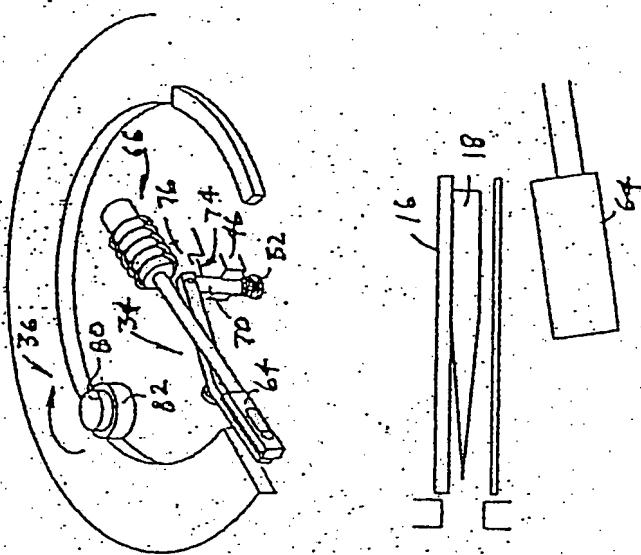


FIG 5

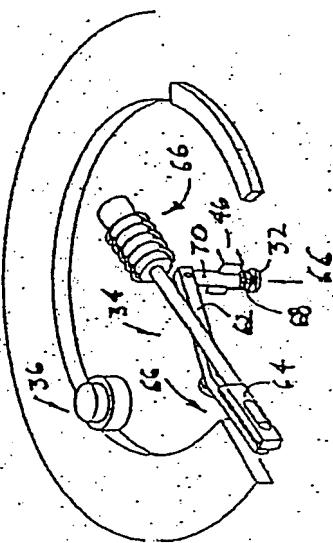


FIG 6B

FIG. 8A

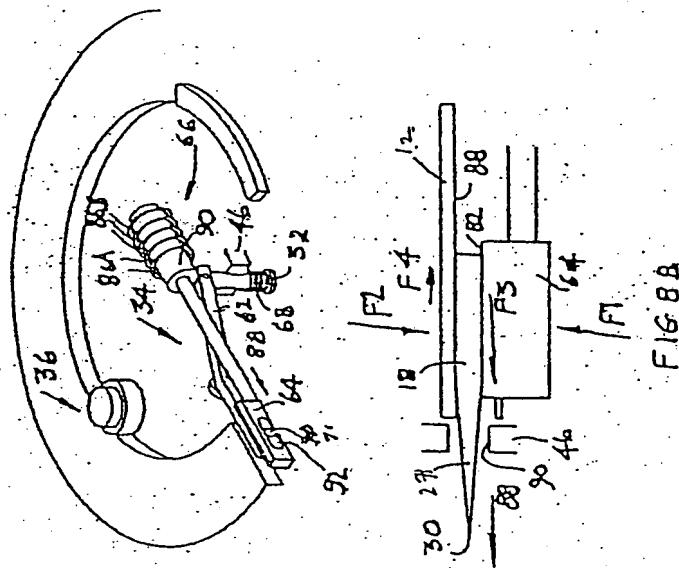
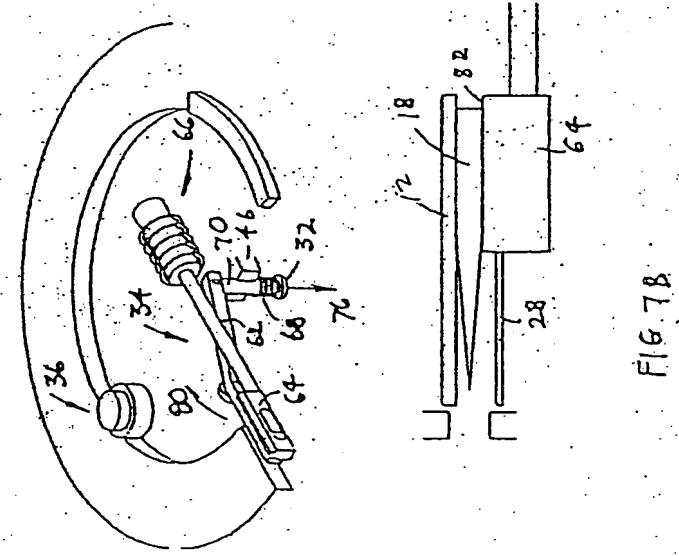


FIG. 7A



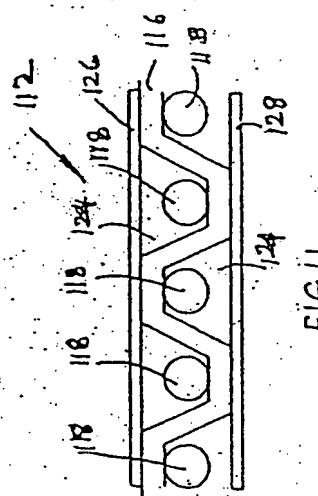


FIG. 11

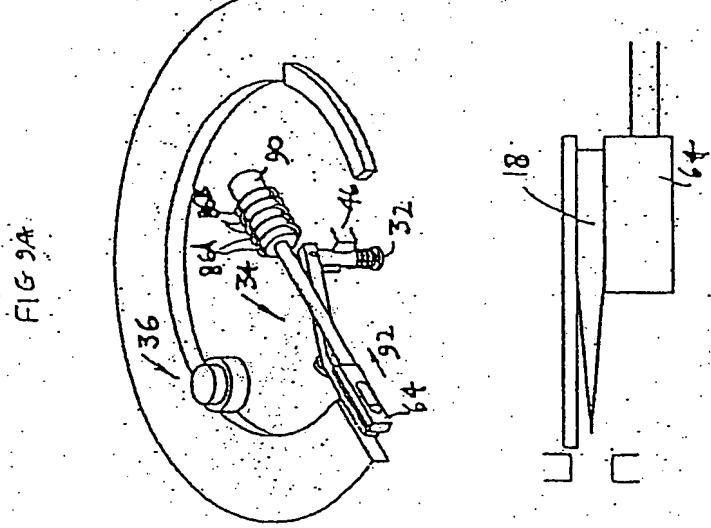


FIG. 9A

FIG. 9B

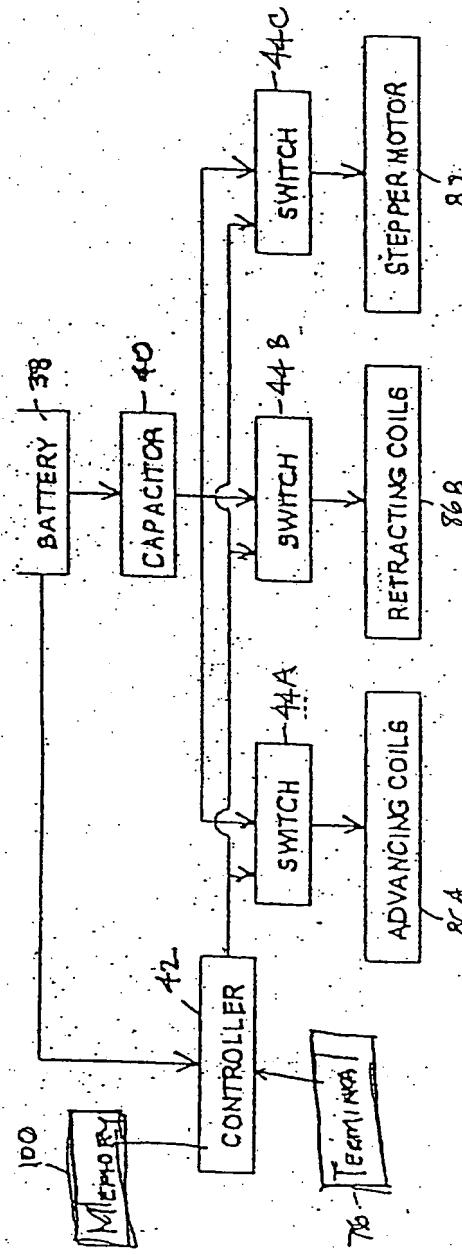


FIG. 10

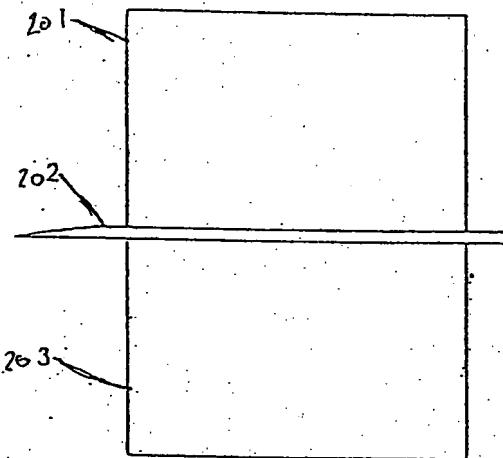


FIG -12

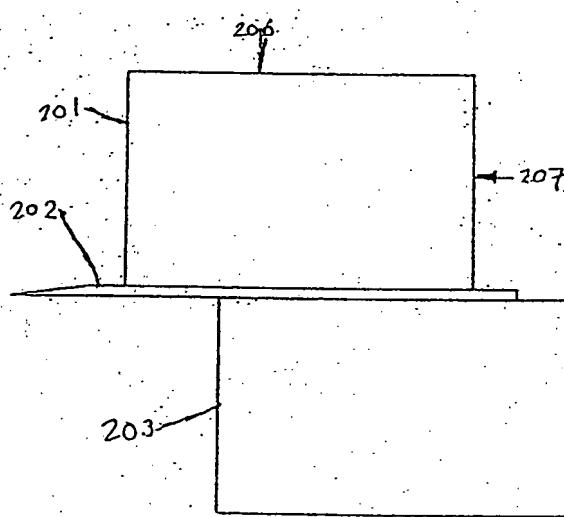


FIG -13

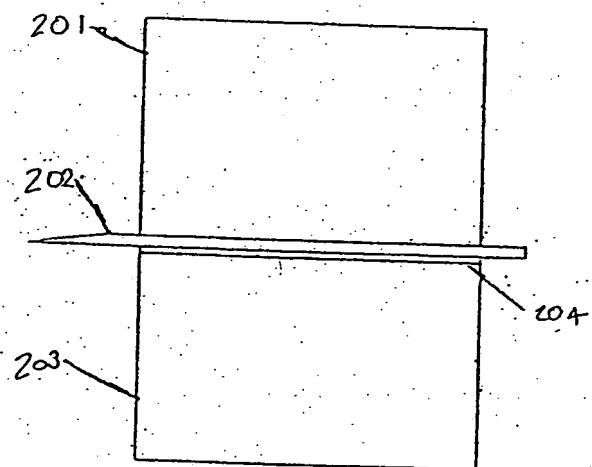


FIG-14

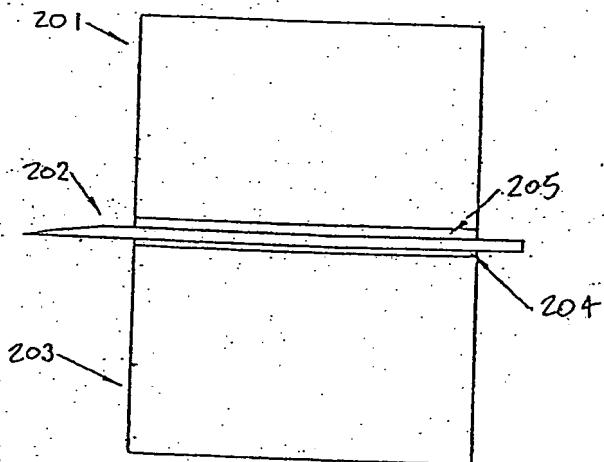
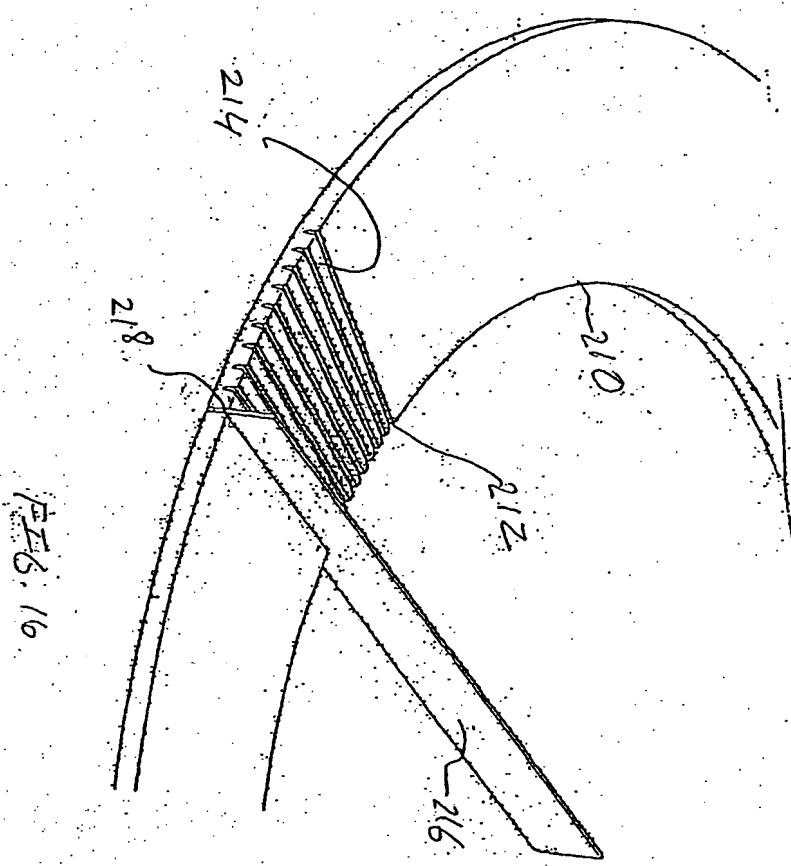
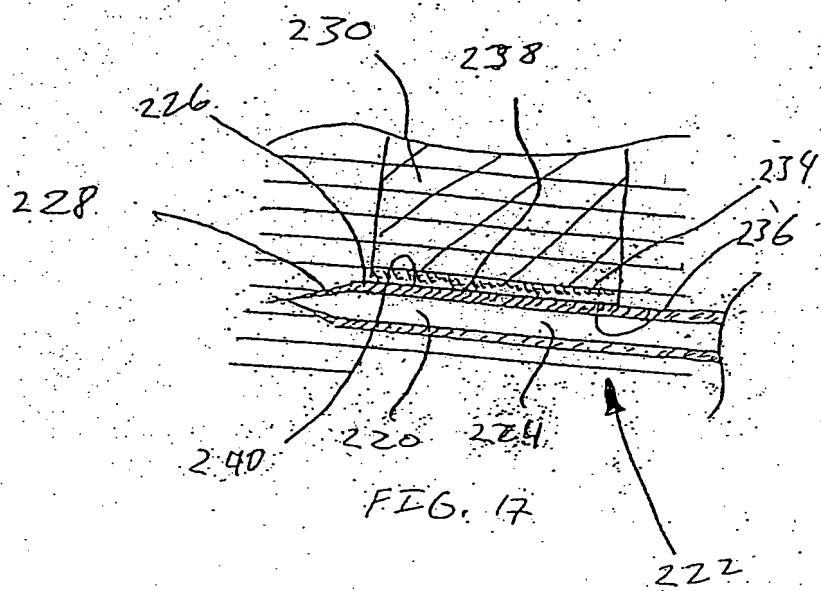


FIG-15





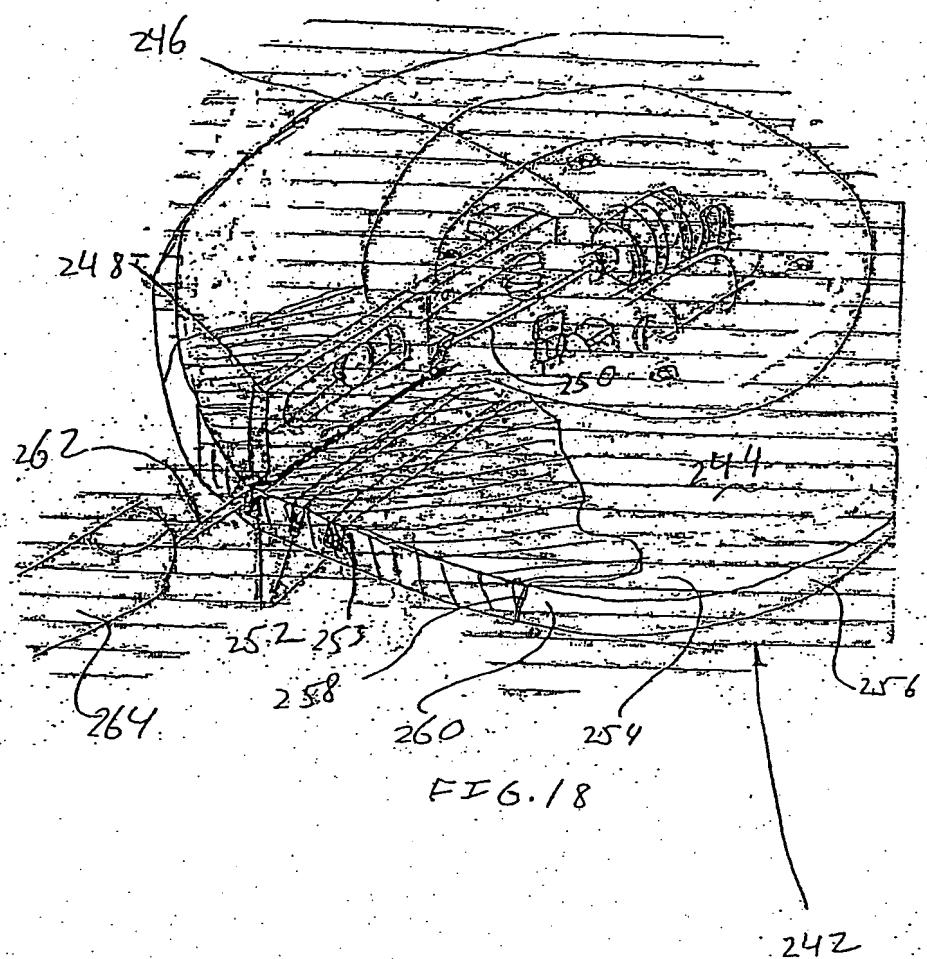
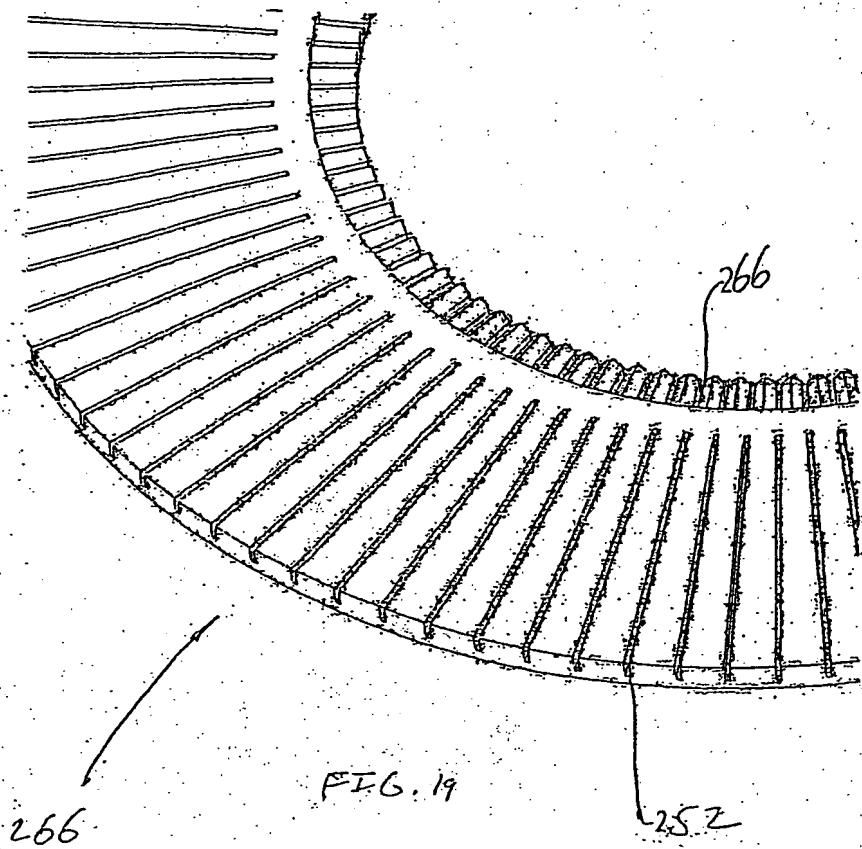


FIG. 18



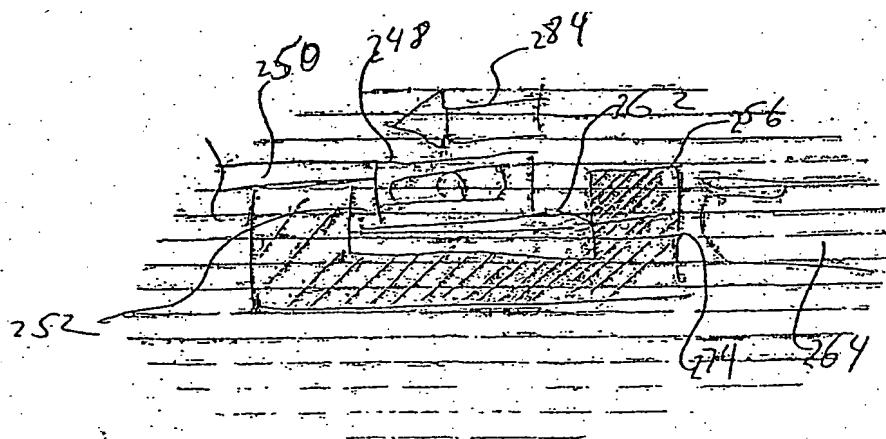
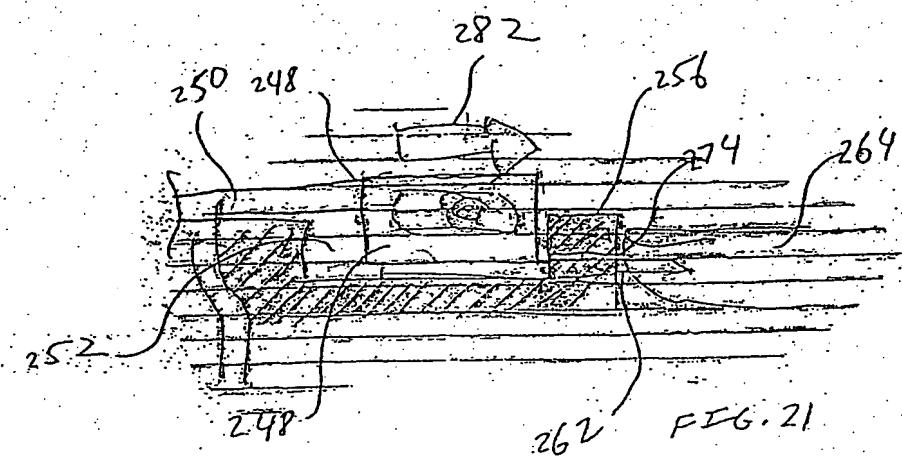
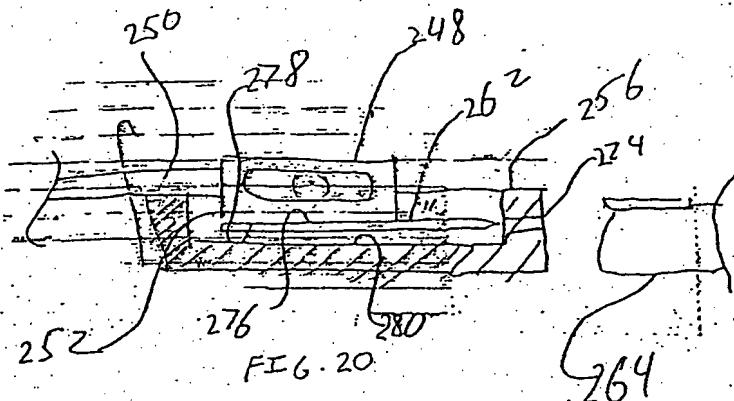


FIG. 22

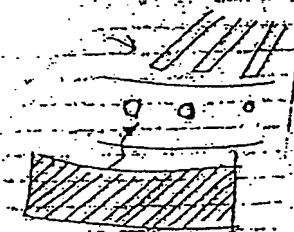
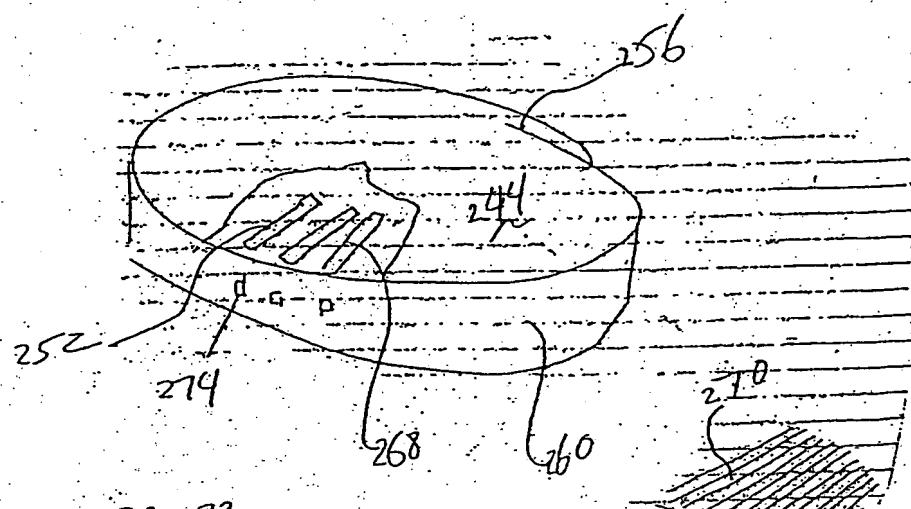


FIG. 25

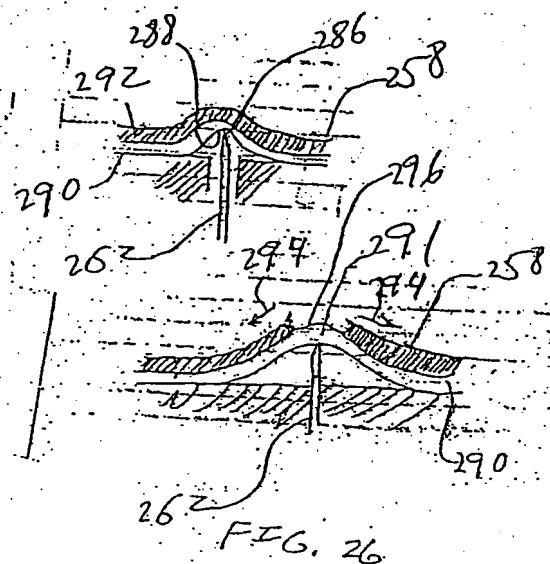


FIG. 26

FIG. 27

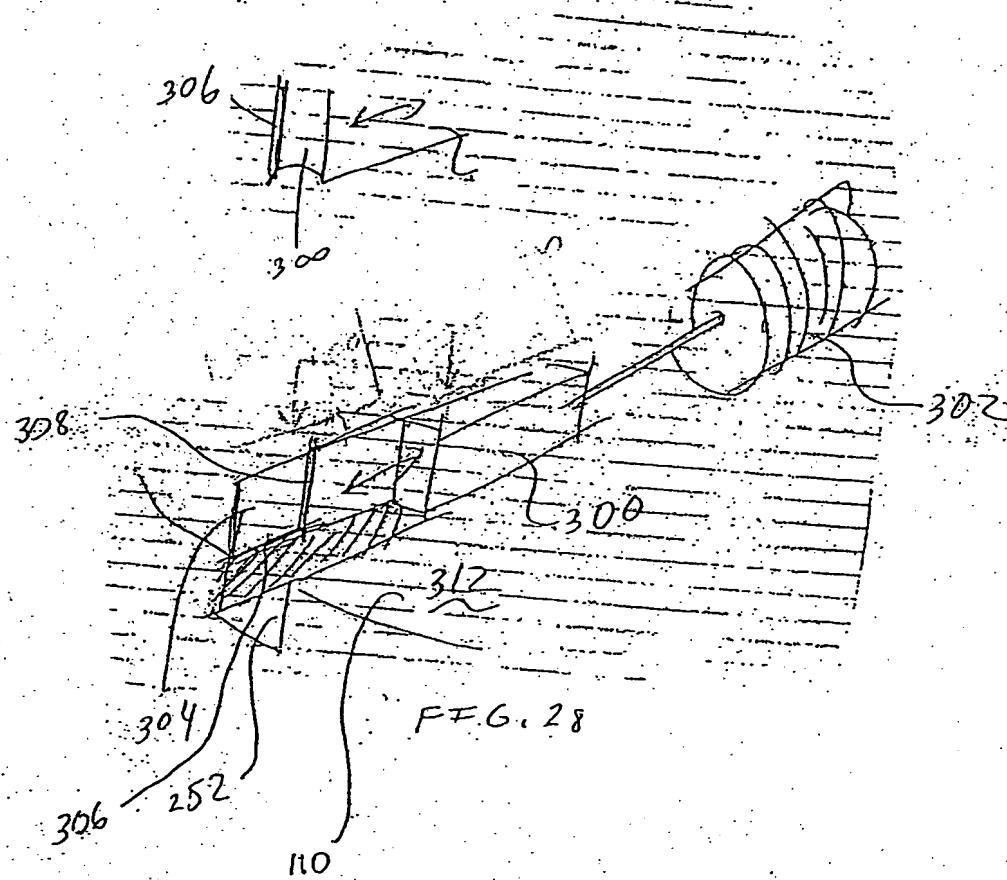


FIG. 28

FIG. 29.

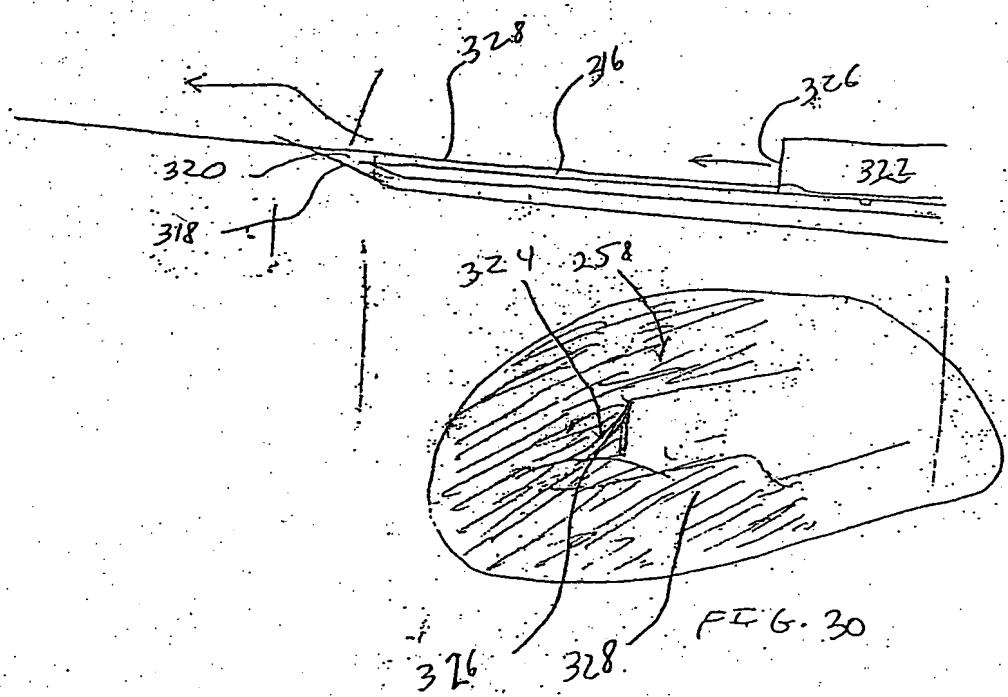
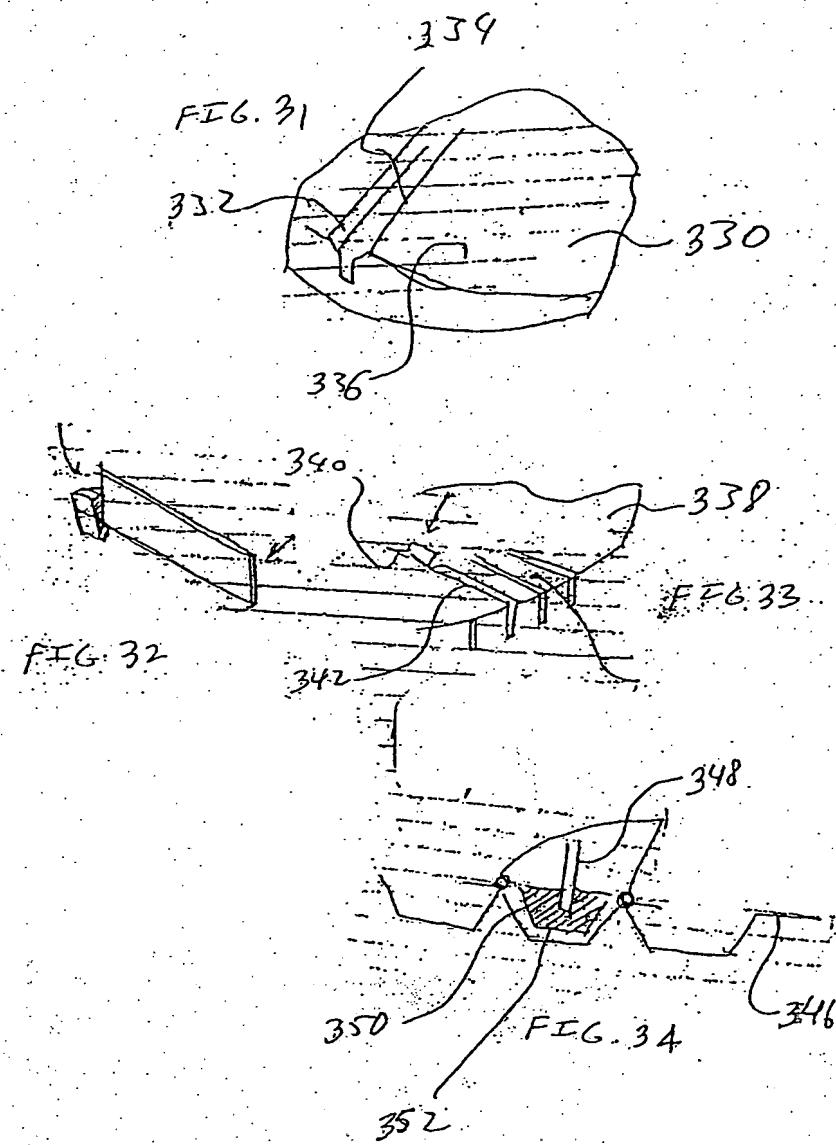
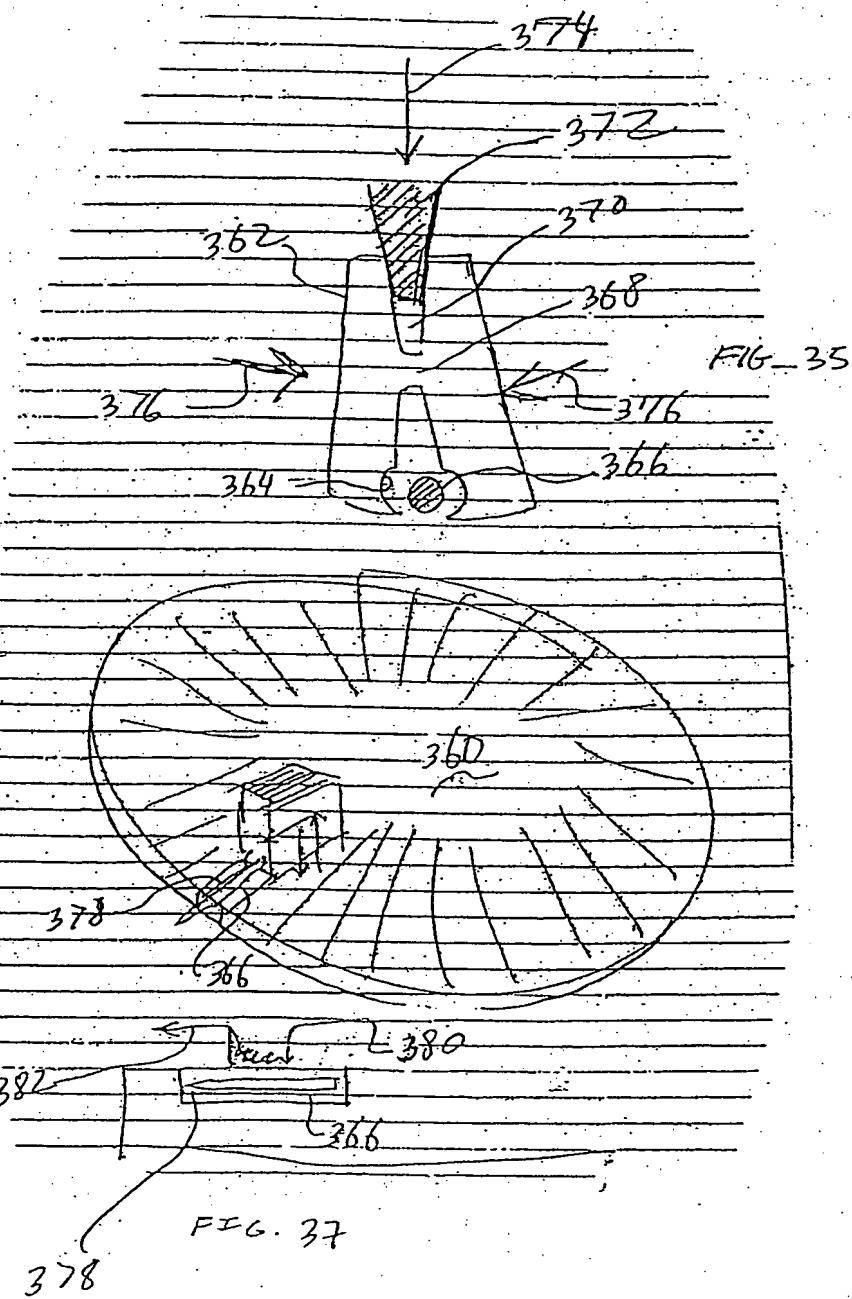


FIG. 30.

326 328

16/115





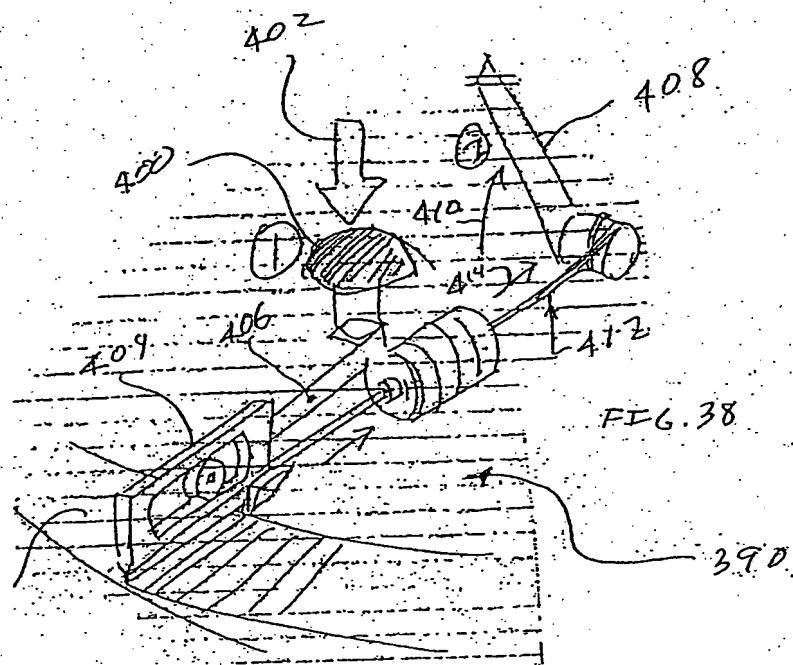


FIG. 38

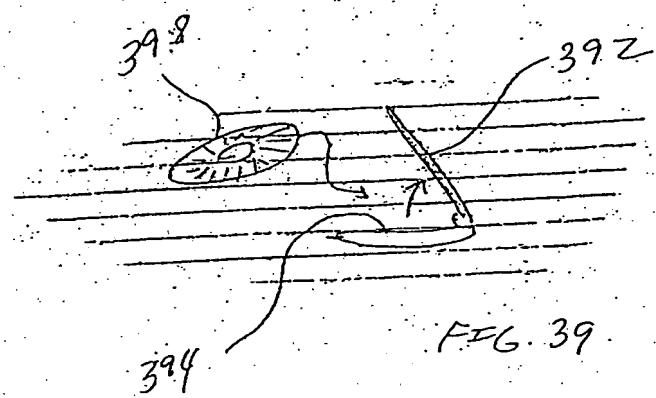
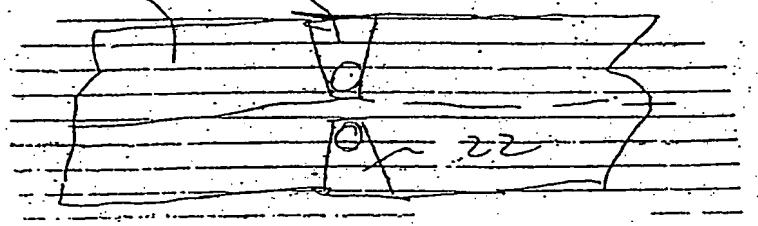


FIG. 39

420 422 FIG. 40



420

422

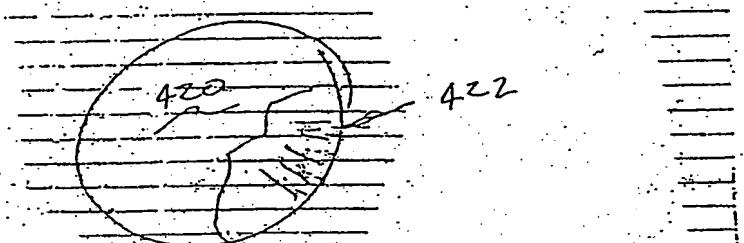


FIG. 41

434

432

FIG. 42

430

436

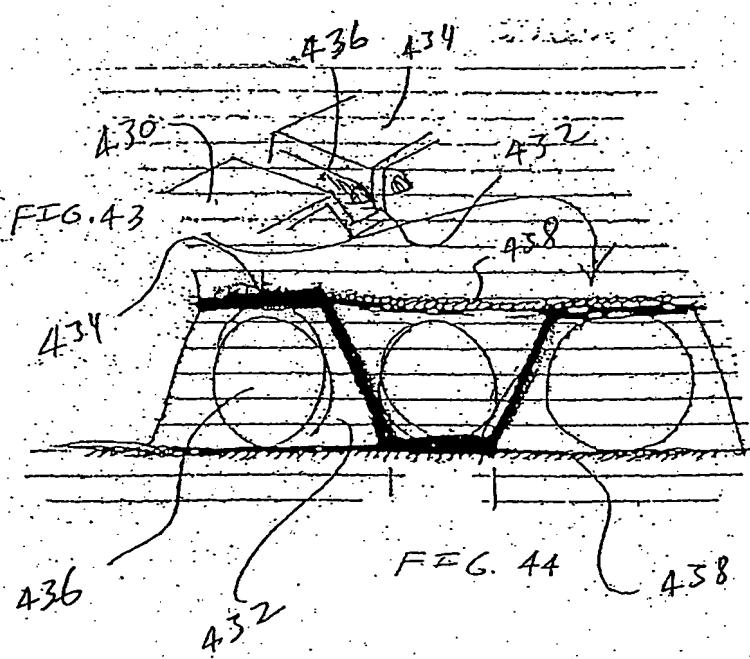


FIG. 45

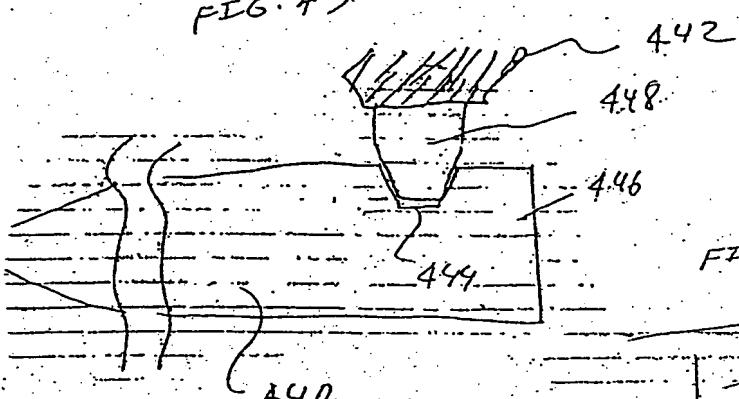


FIG. 46

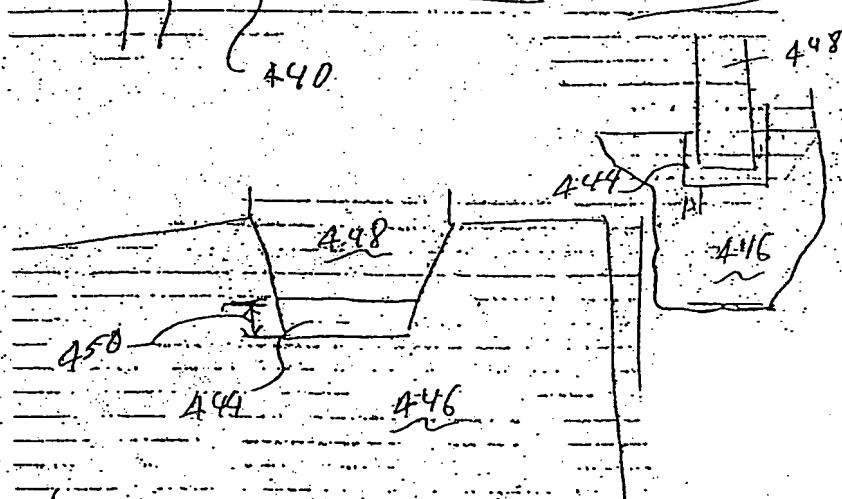
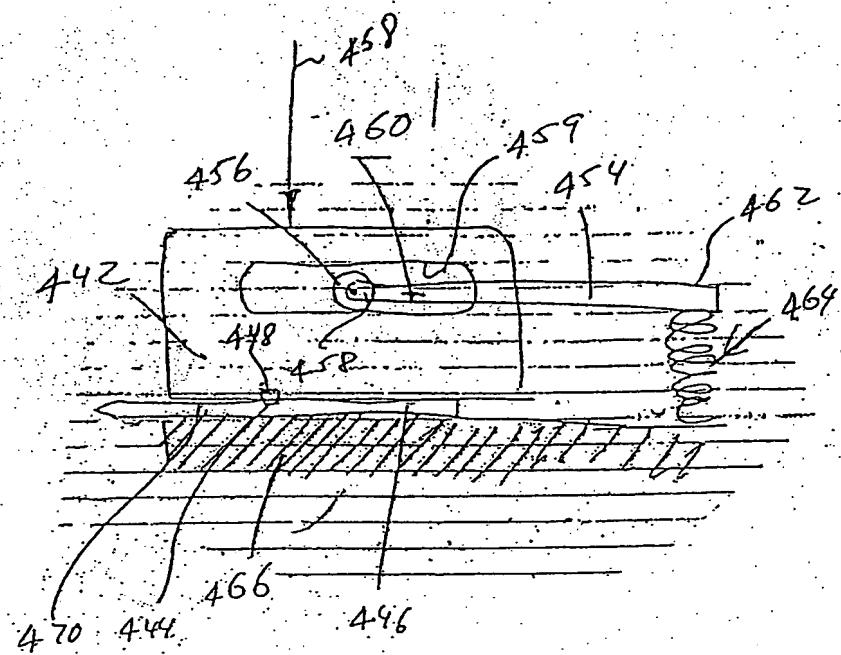
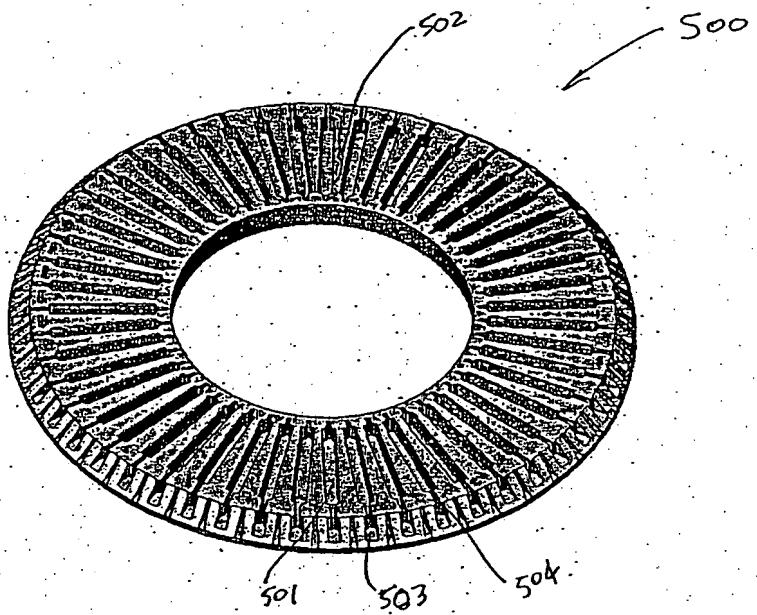


FIG. 47





FIG_ 49

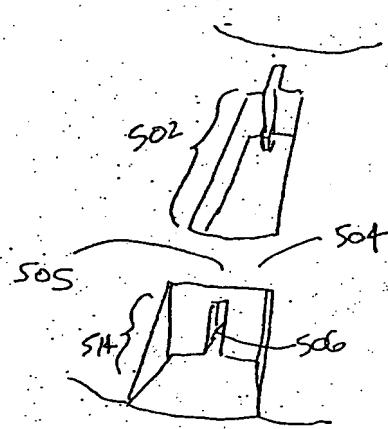


FIG-50

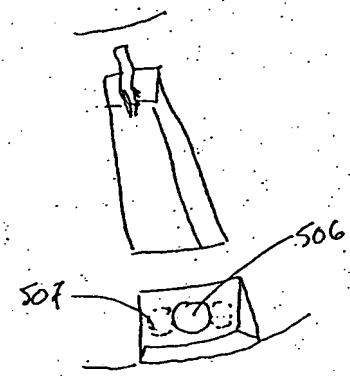


FIG-51

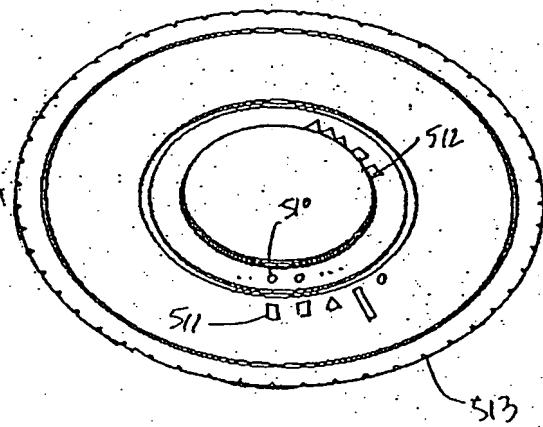


FIG-52

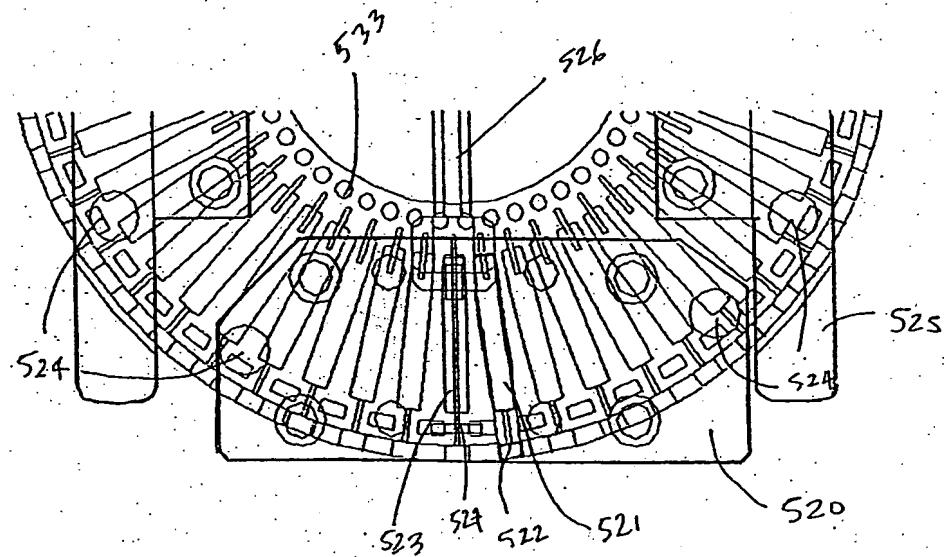


FIG-53A

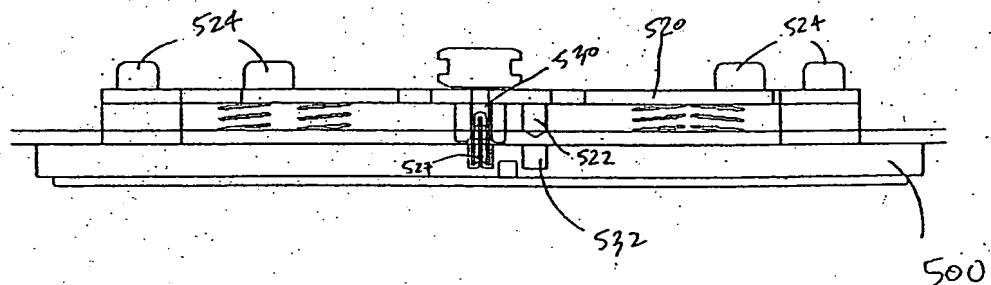


FIG-54A

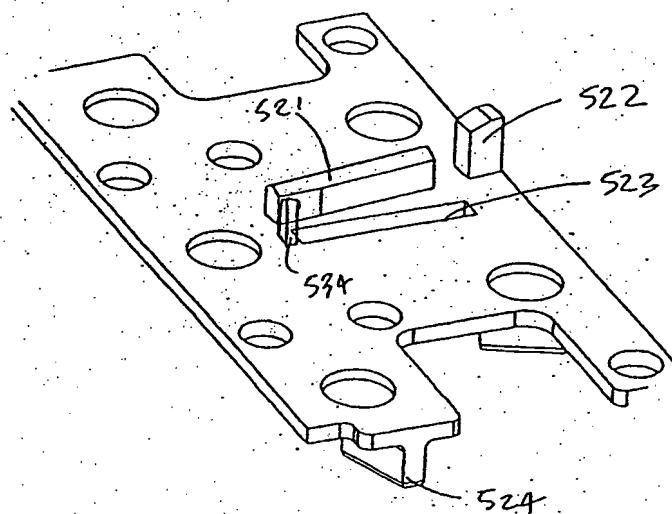


FIG-S3B

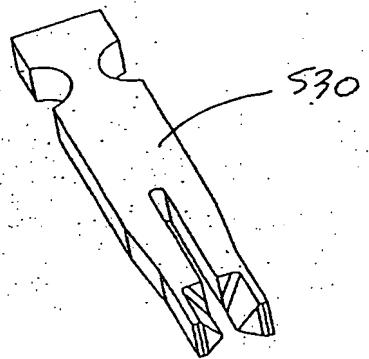


FIG-S4B

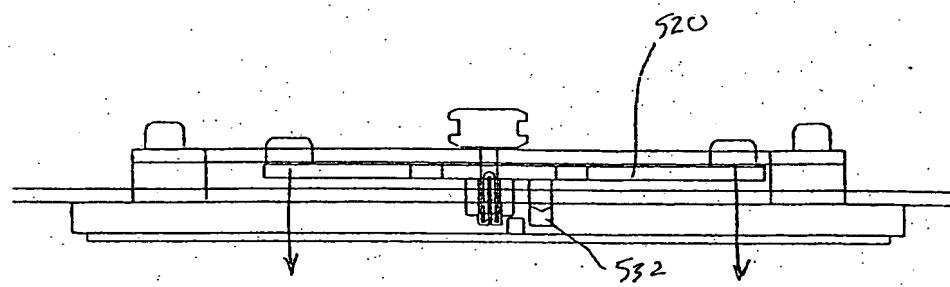


FIG-54C

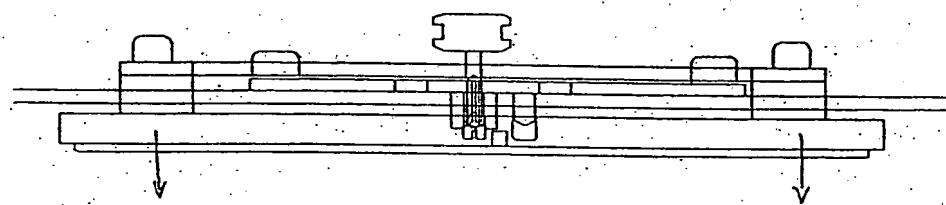


FIG-54D

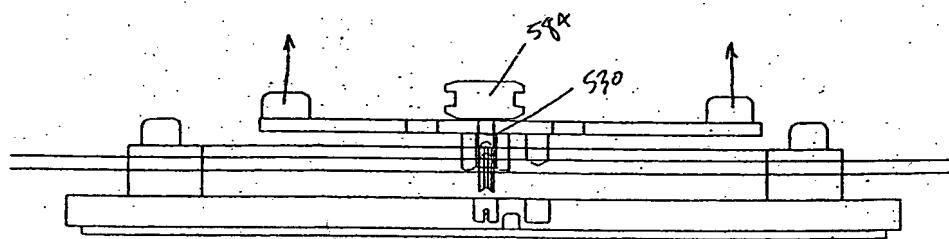
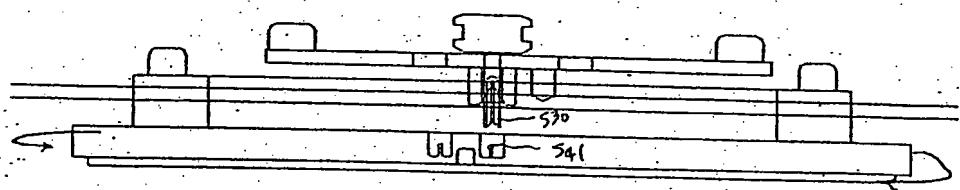
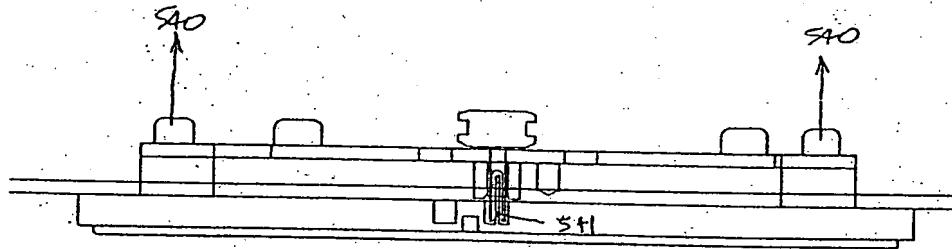


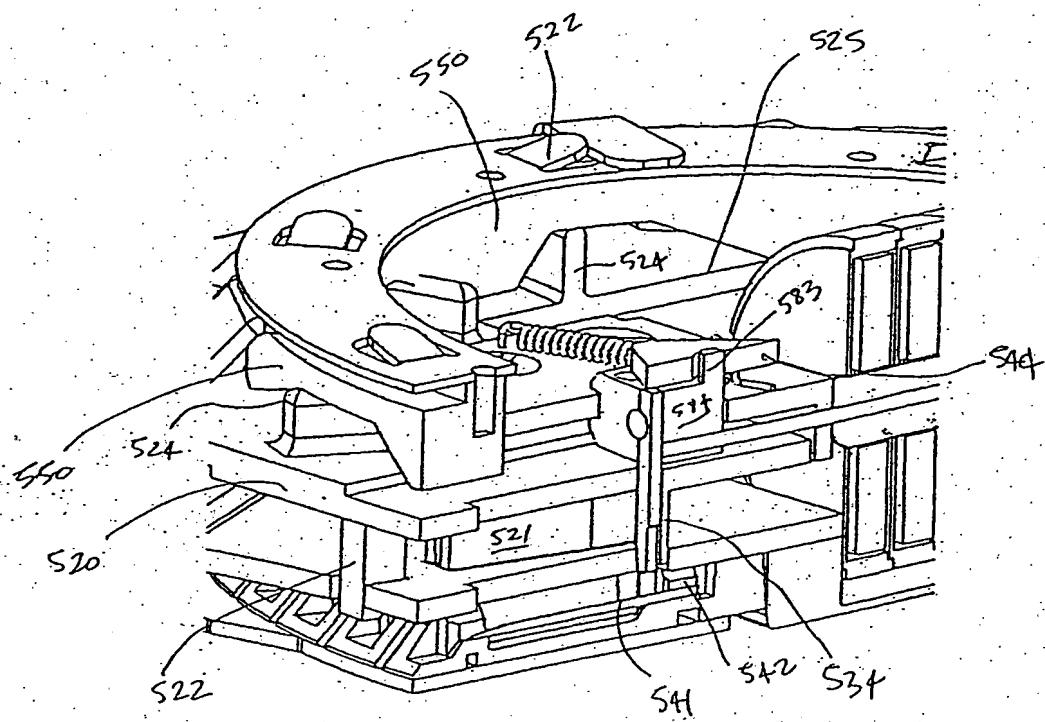
FIG-54E



FIG_S4F



FIG_S4G



FIG_55A

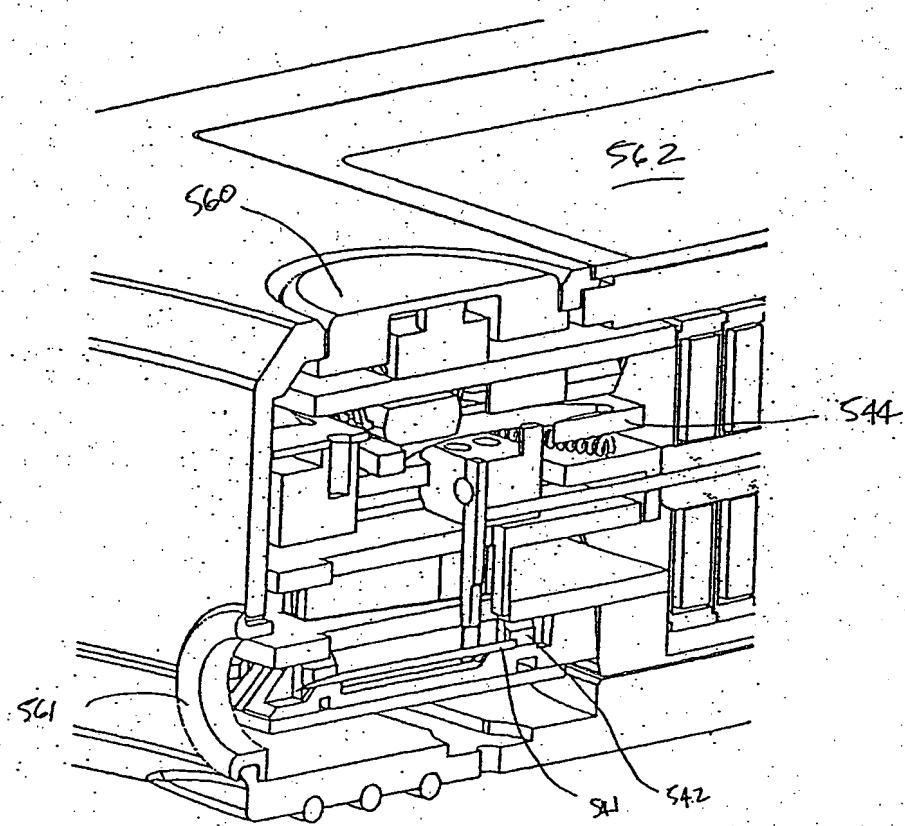


FIG - SSB

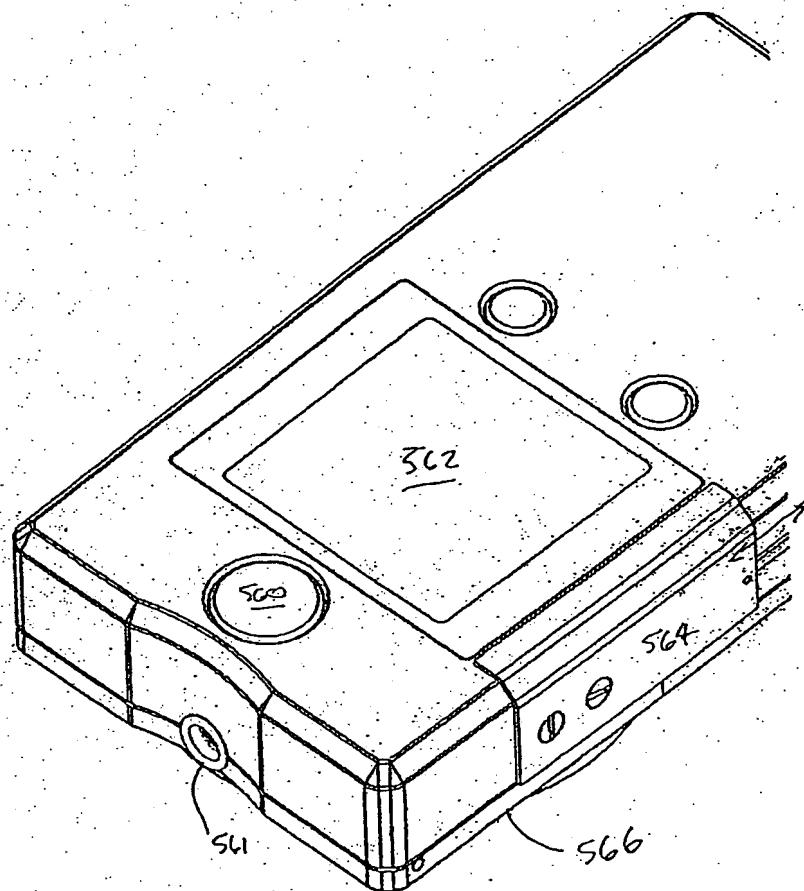


FIG - 56A

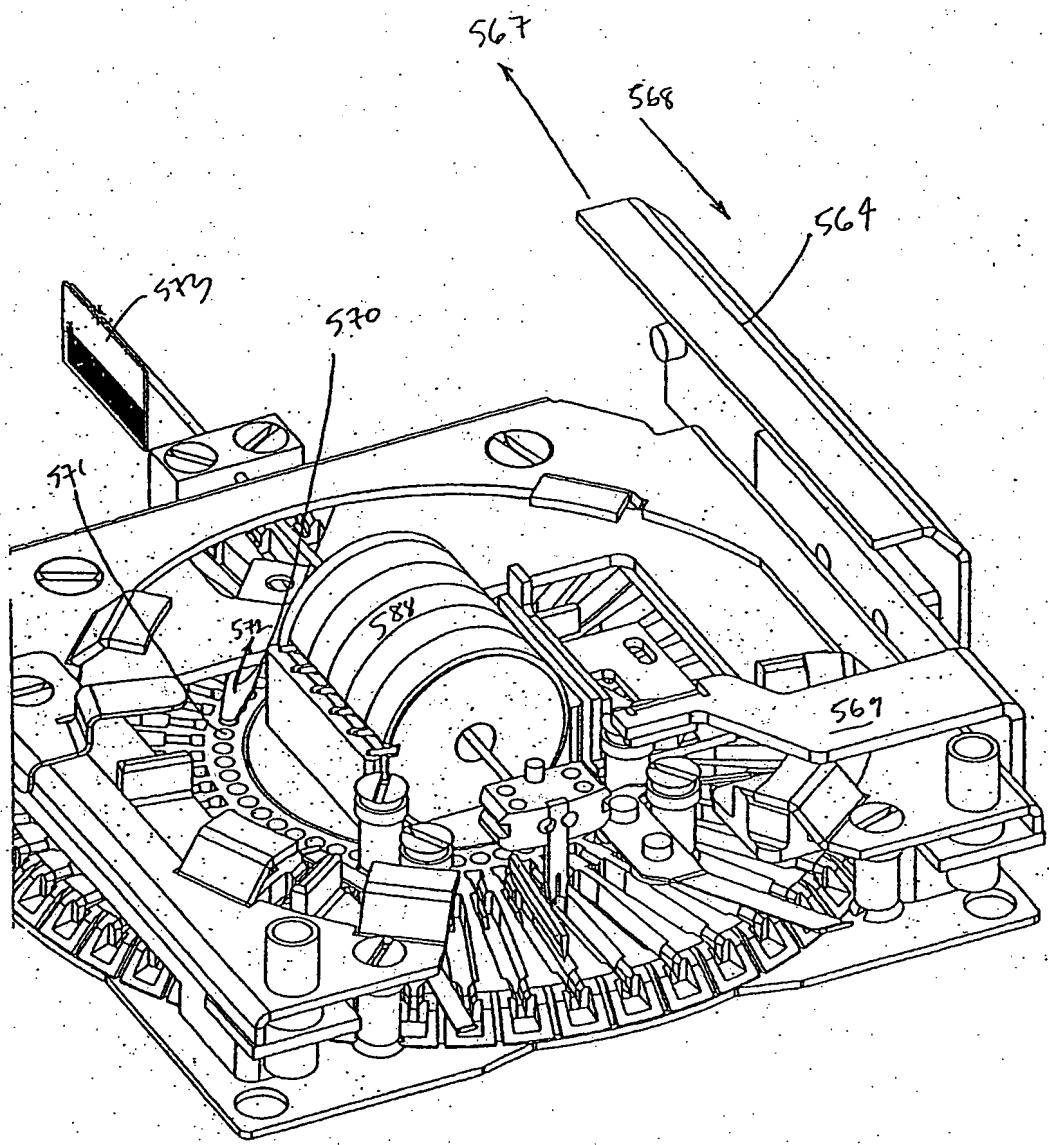


FIG-56B

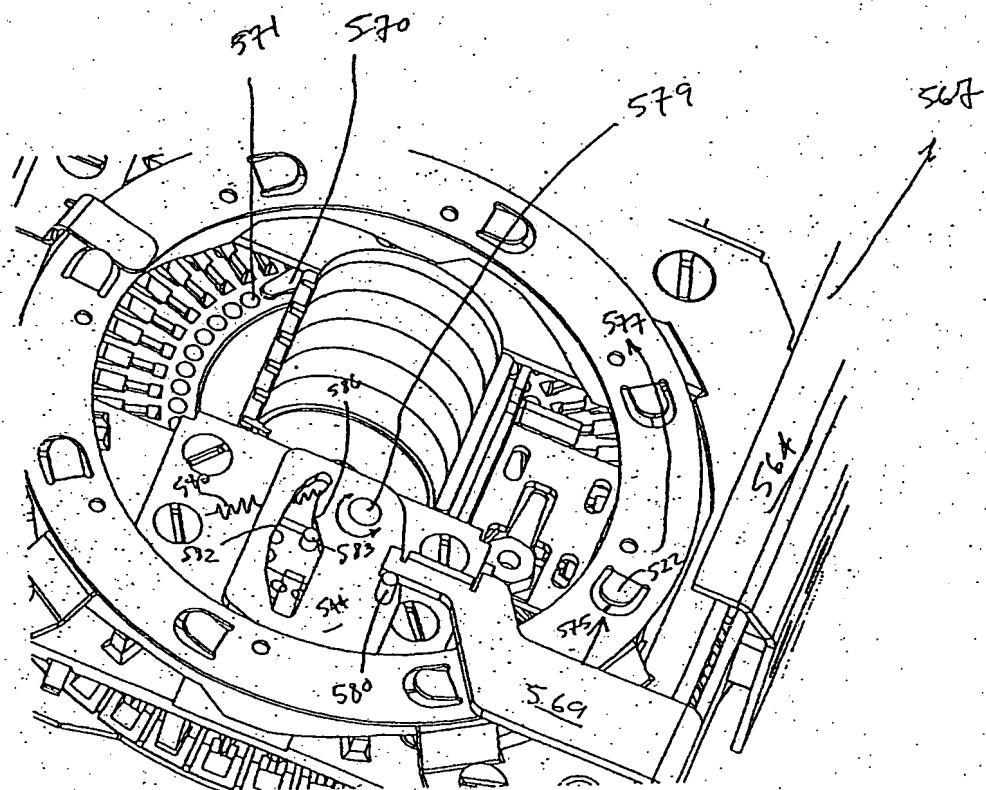


FIG. 56C

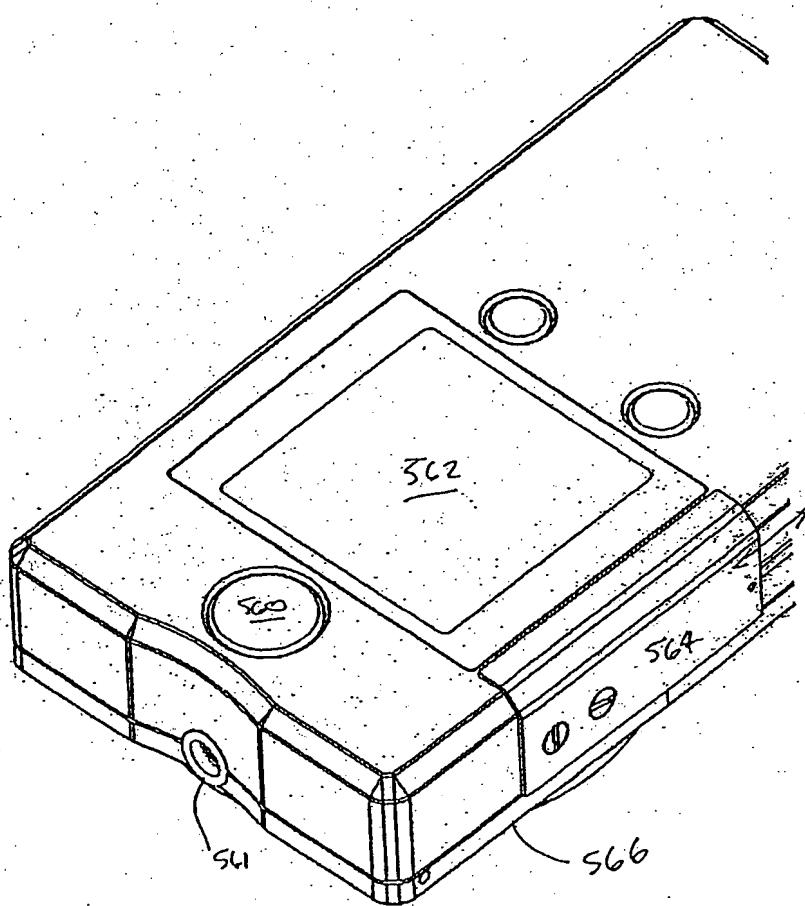


FIG - 56A

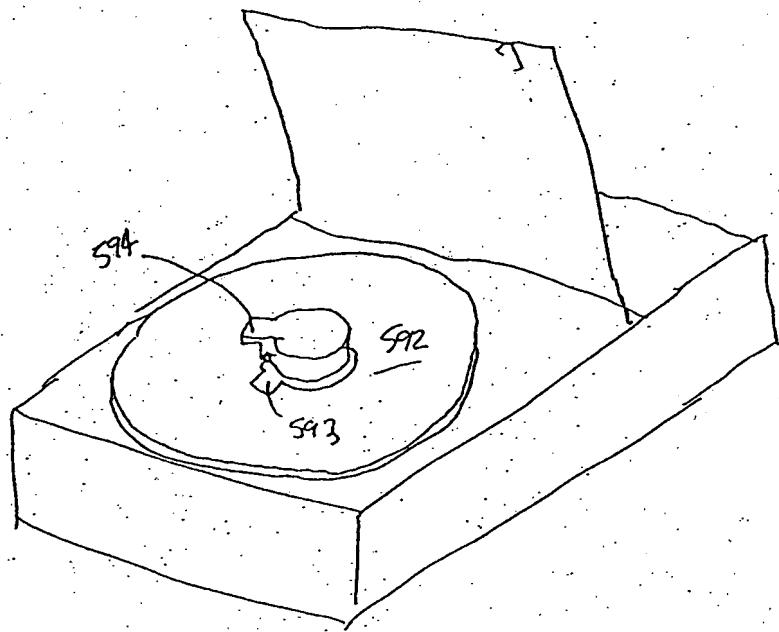


FIG. 56 D

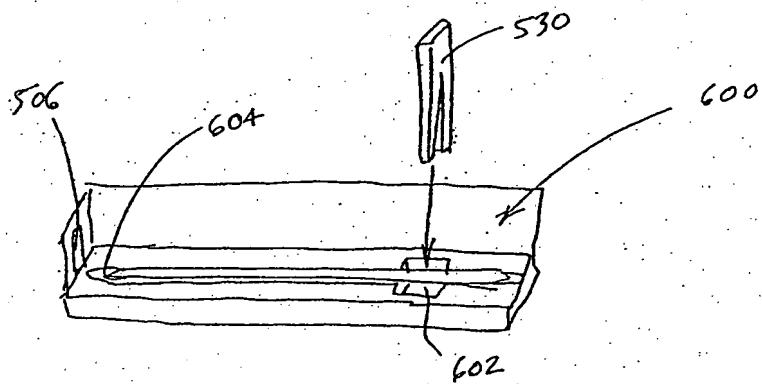


FIG - 57

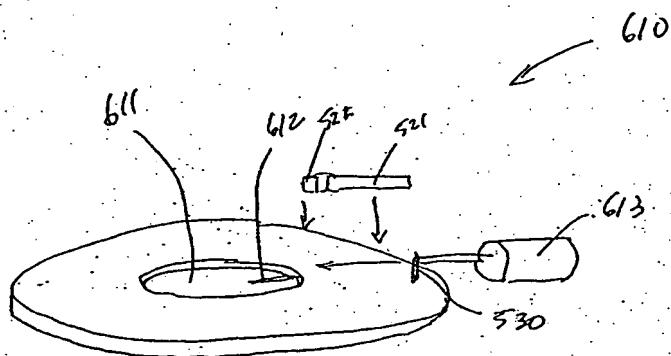


FIG-58

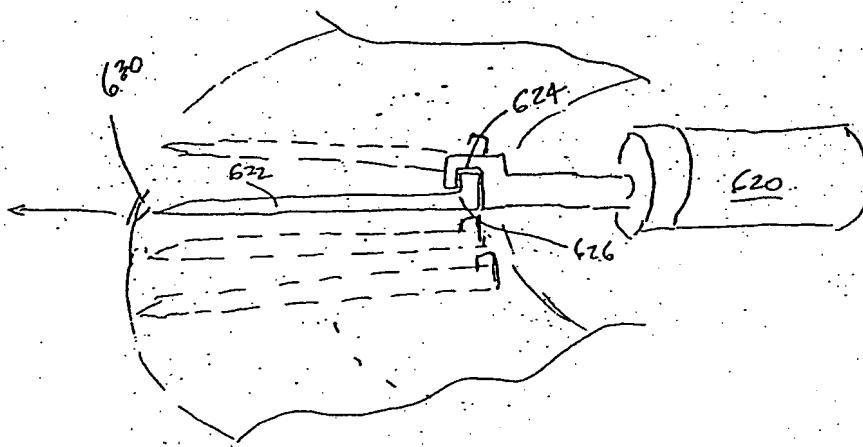


Fig - 59

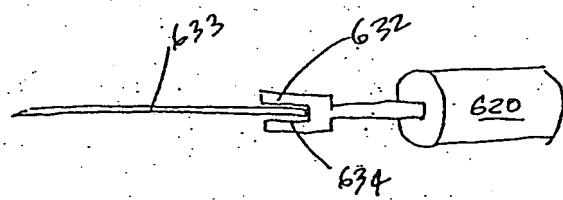


FIG-60A

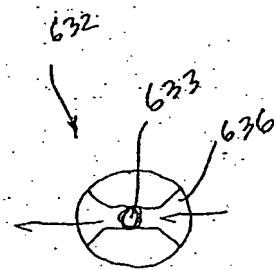


FIG-60B

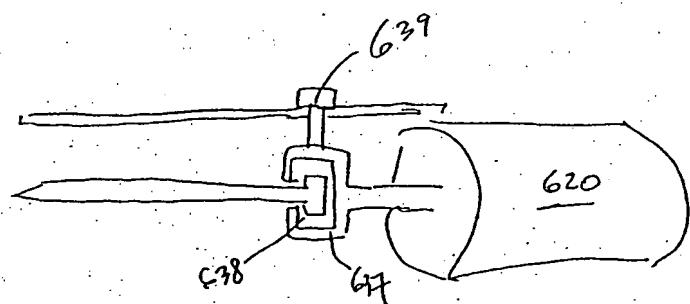


FIG - 60C

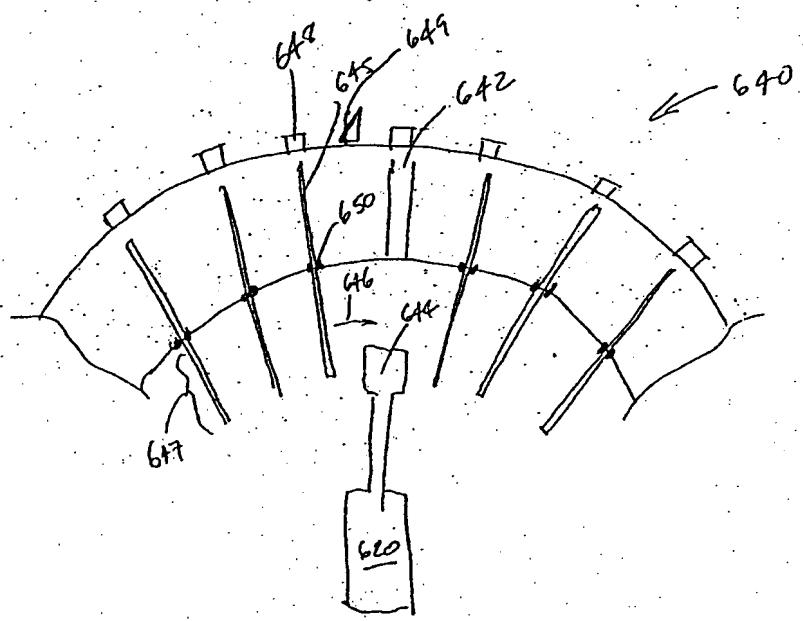


FIG - 61

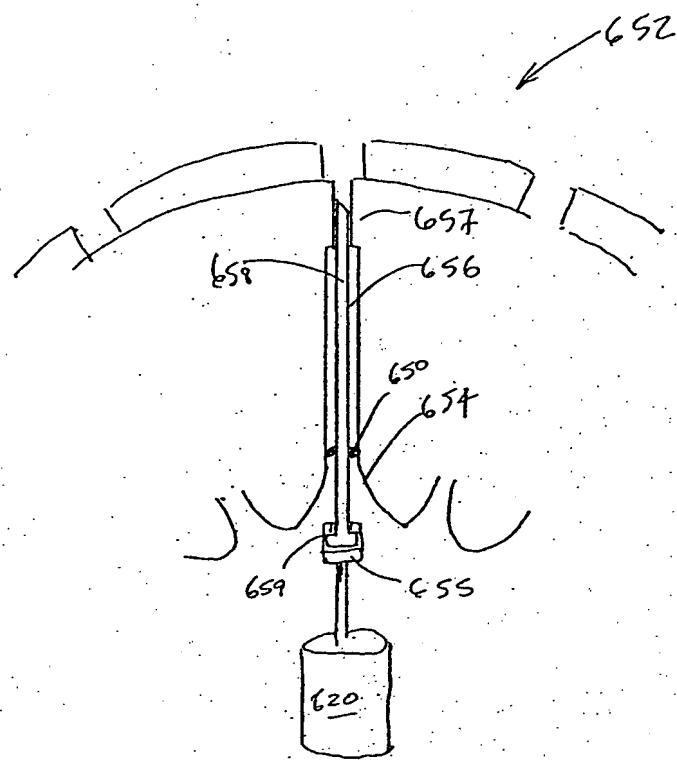


FIG-62

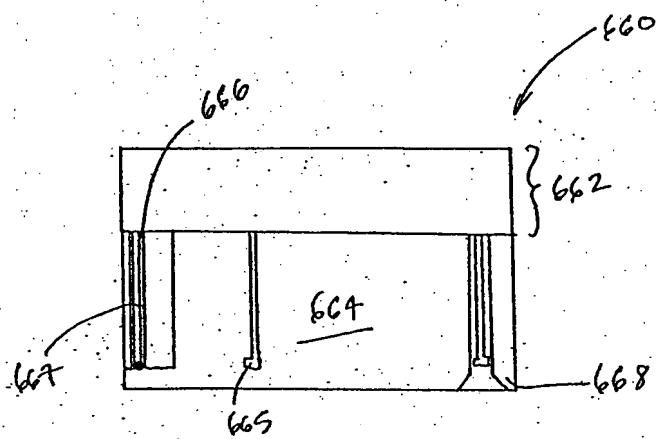


FIG - 63

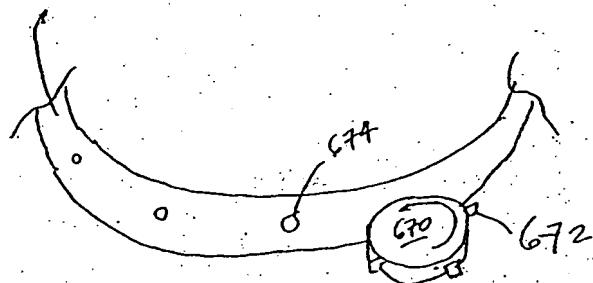


FIG-64A

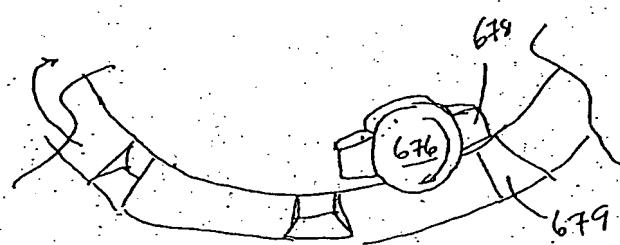


FIG-64B

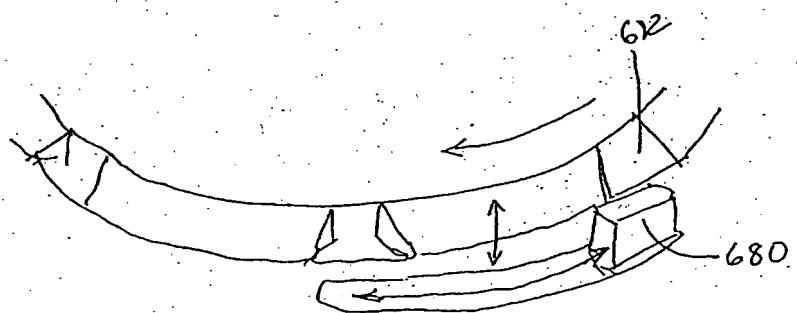


FIG-64C

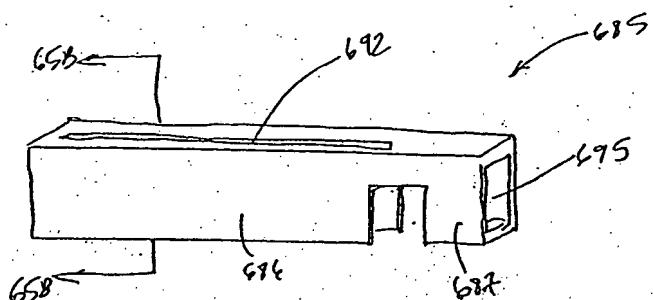


FIG - 65A

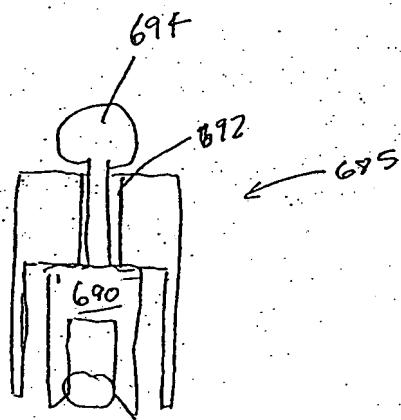


FIG - 65B

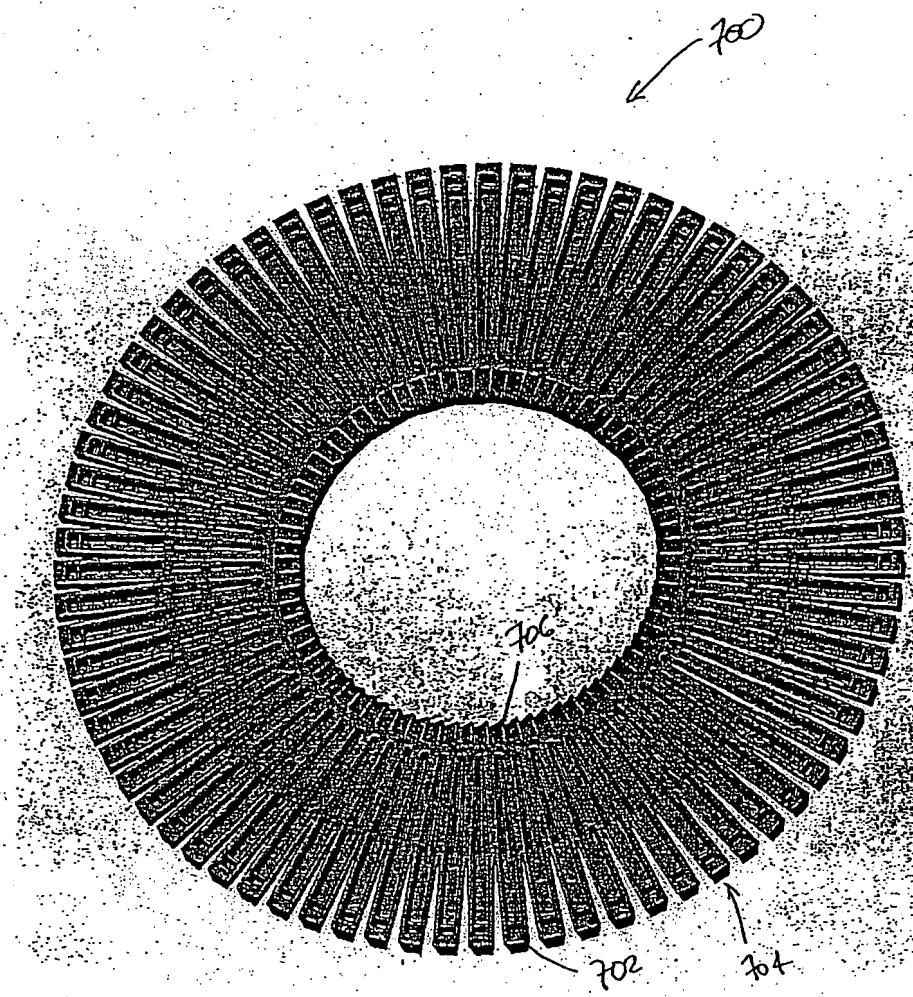


FIG-66

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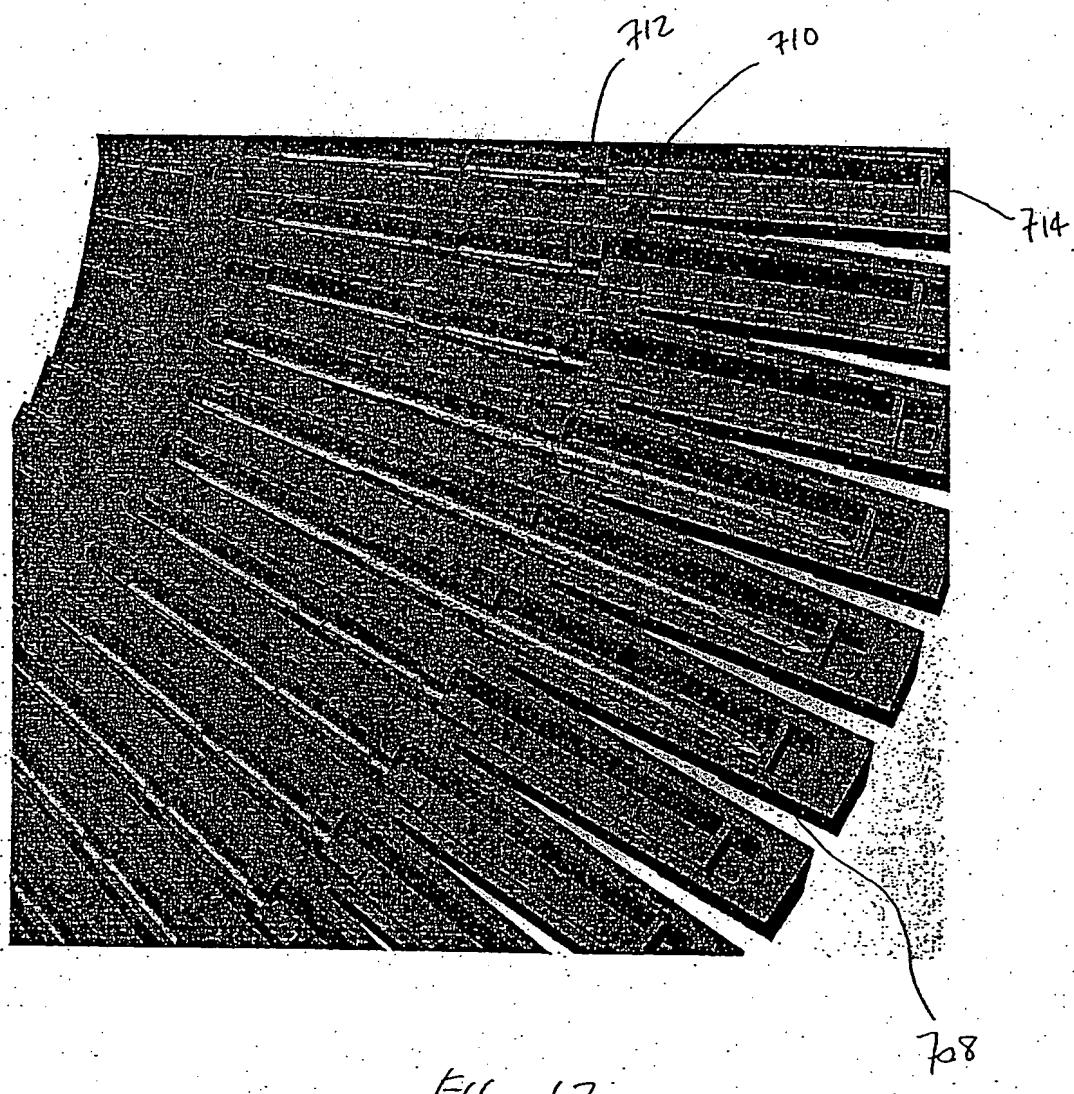


FIG - 67

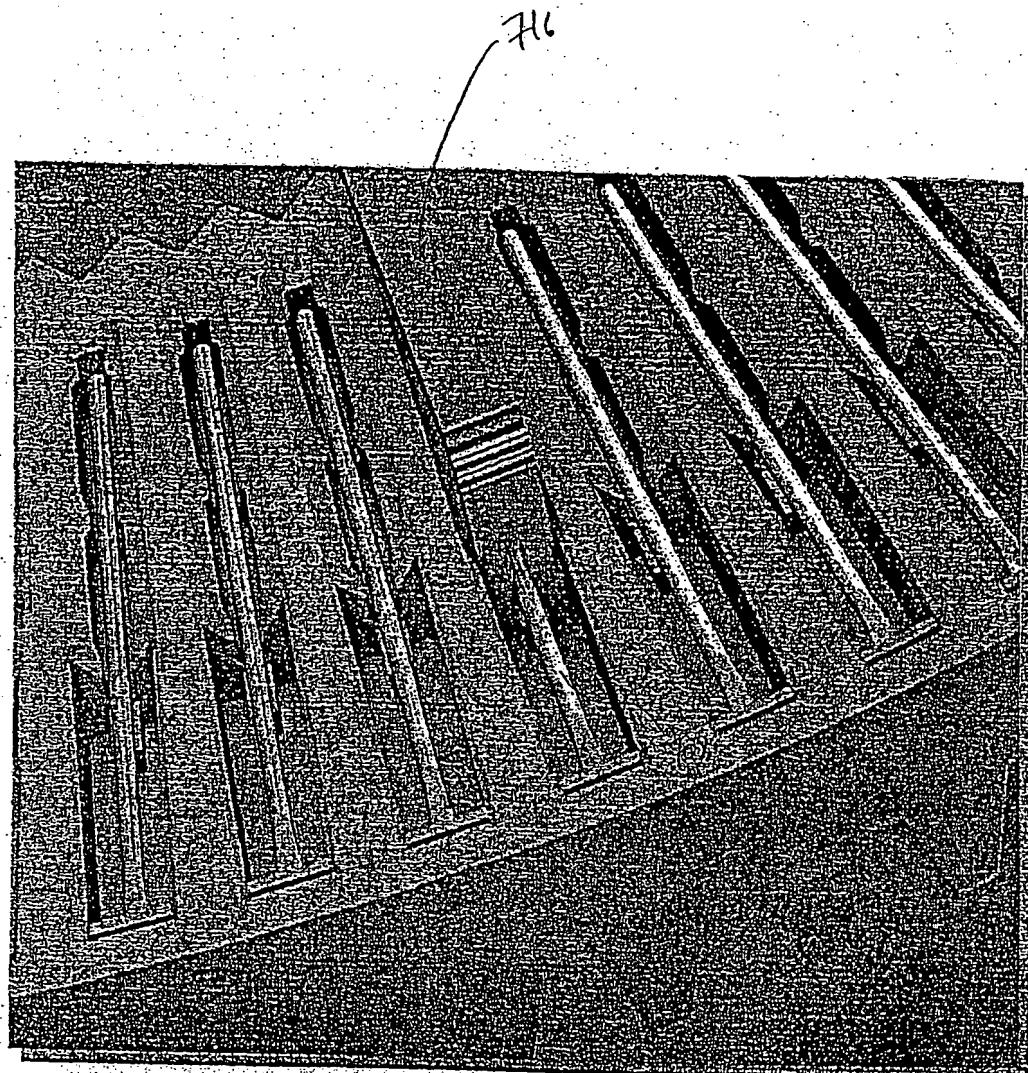


FIG-6

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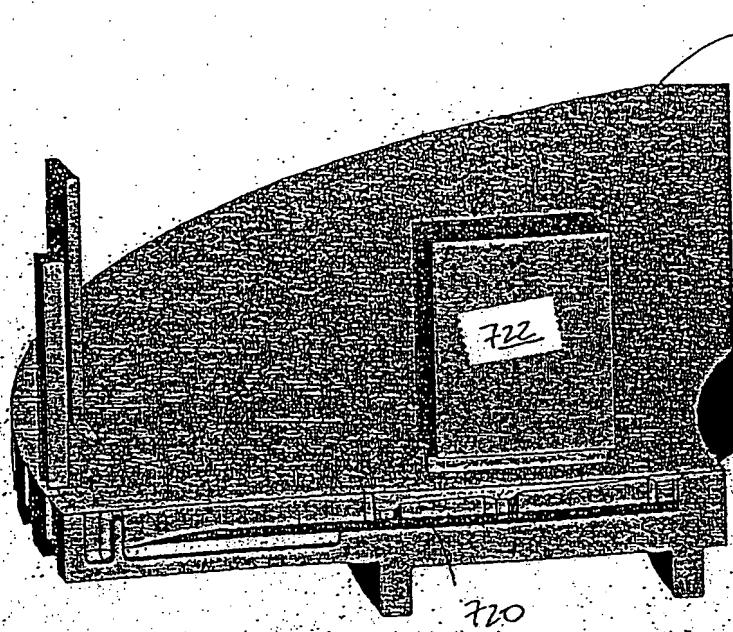


FIG - 69A

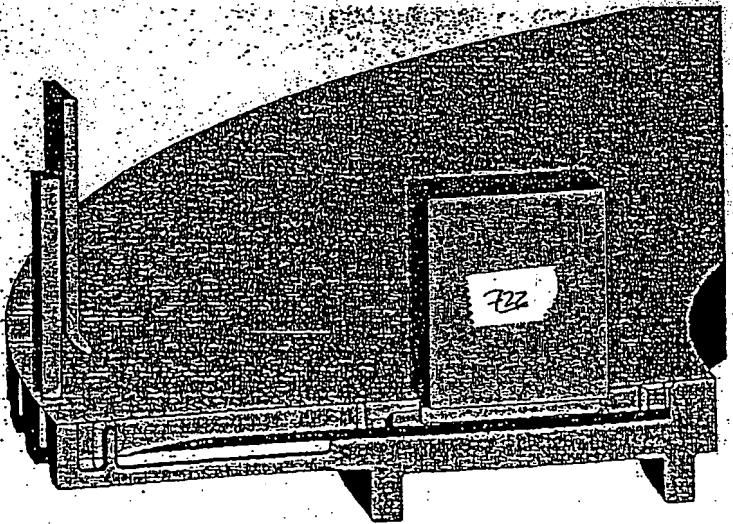


FIG - 69B

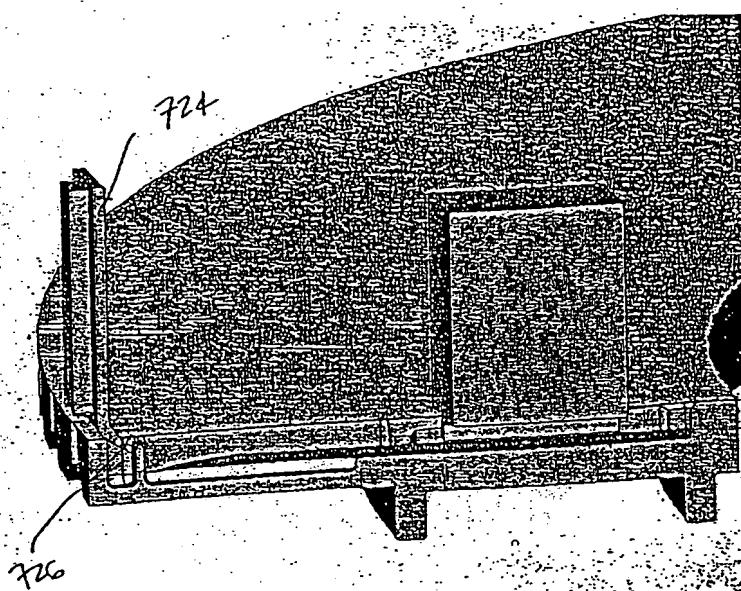


FIG-69C

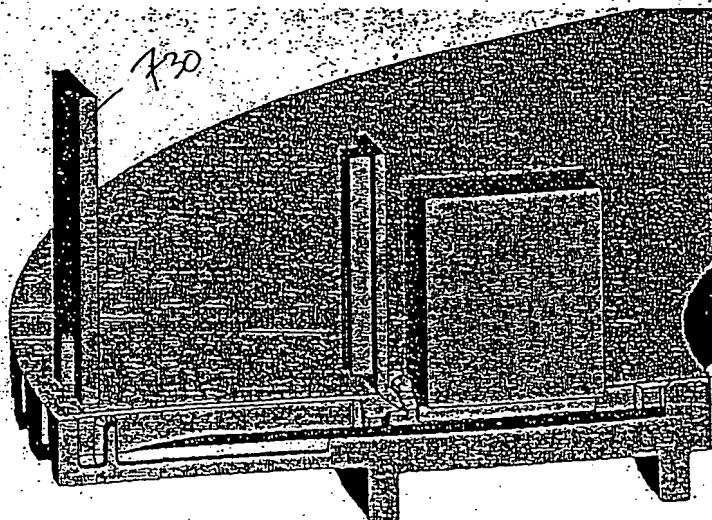


FIG-69D

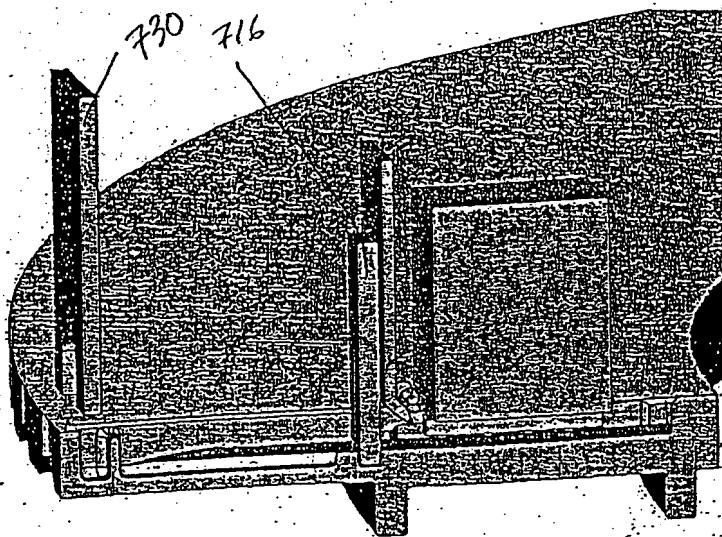


FIG-69E

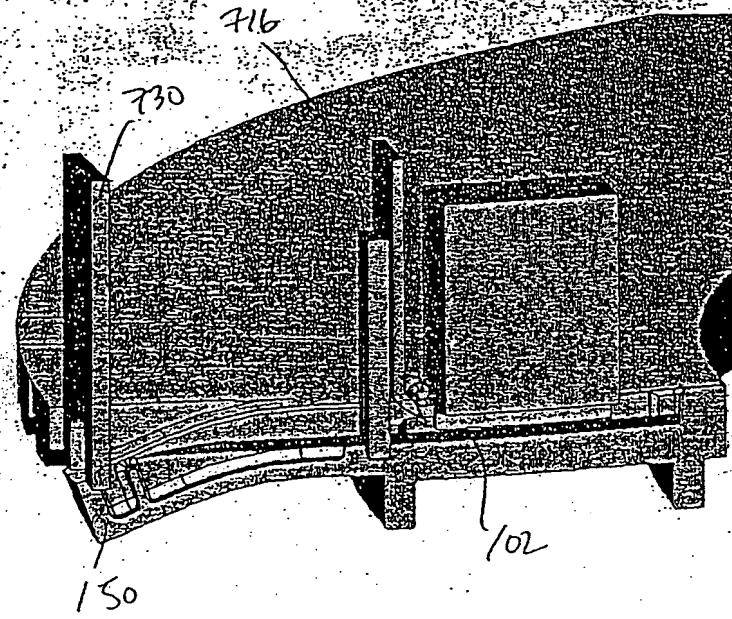


FIG-69F

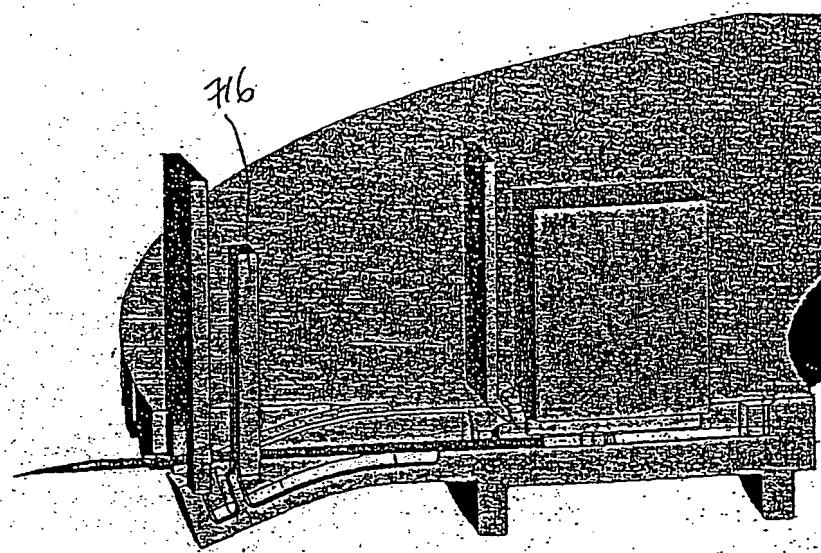


FIG - 69G

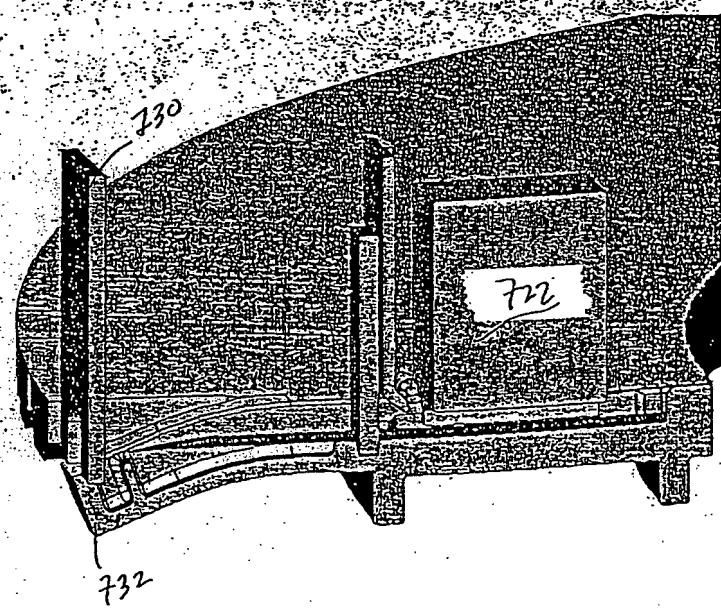


FIG - 69H

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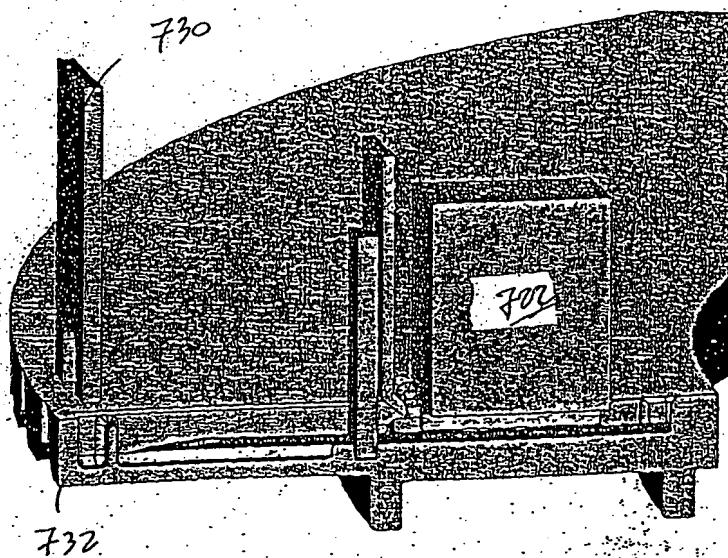


FIG-69I

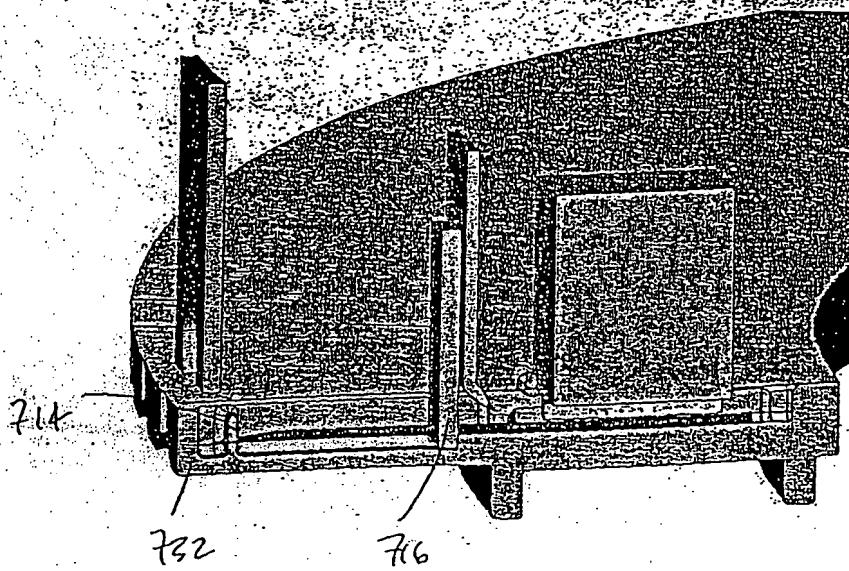


FIG - 69J

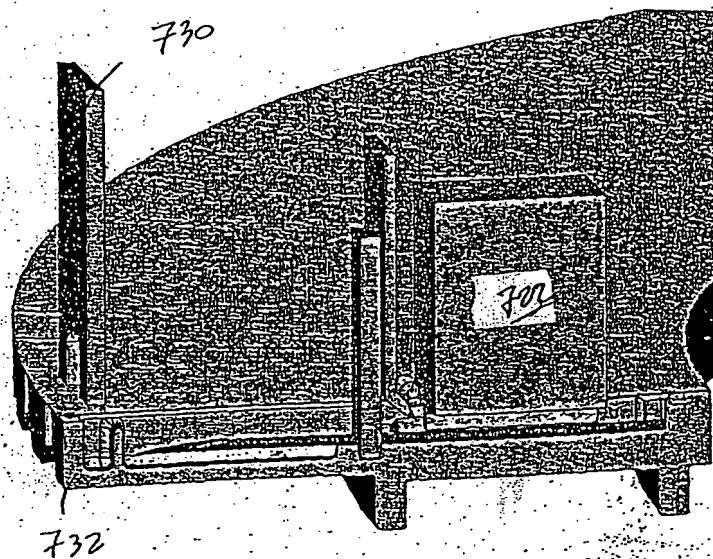


FIG-69I

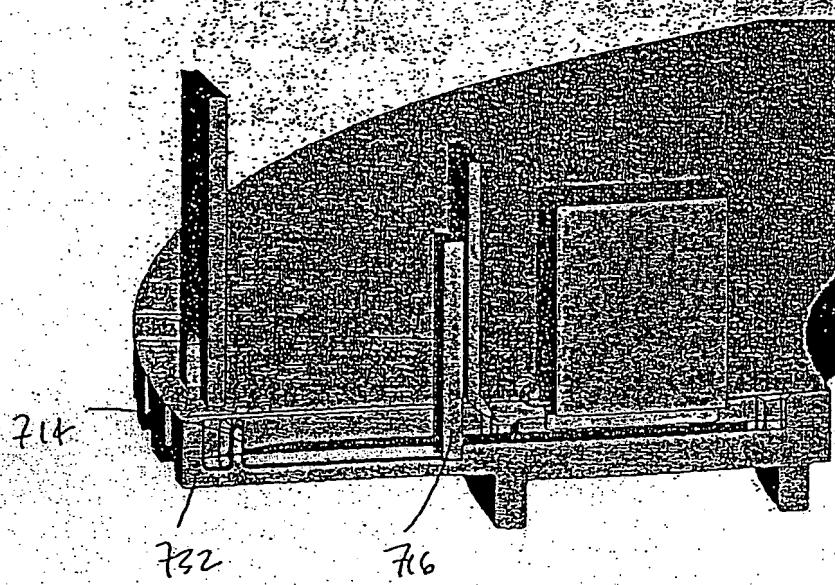


FIG-69J

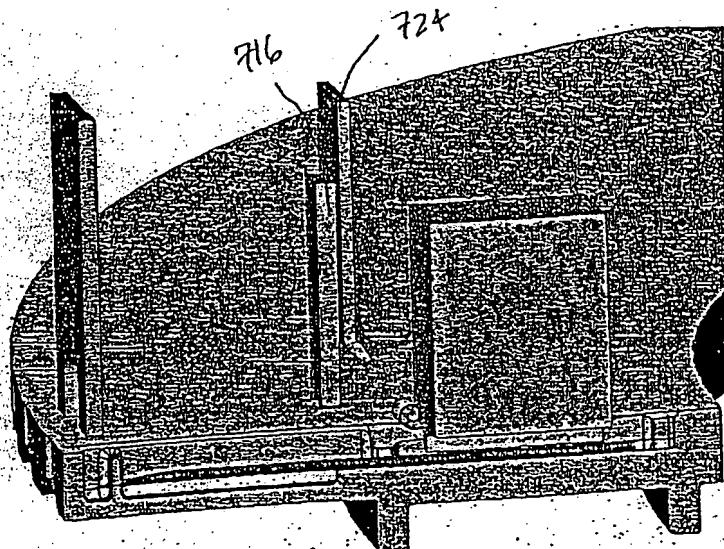


FIG-69K

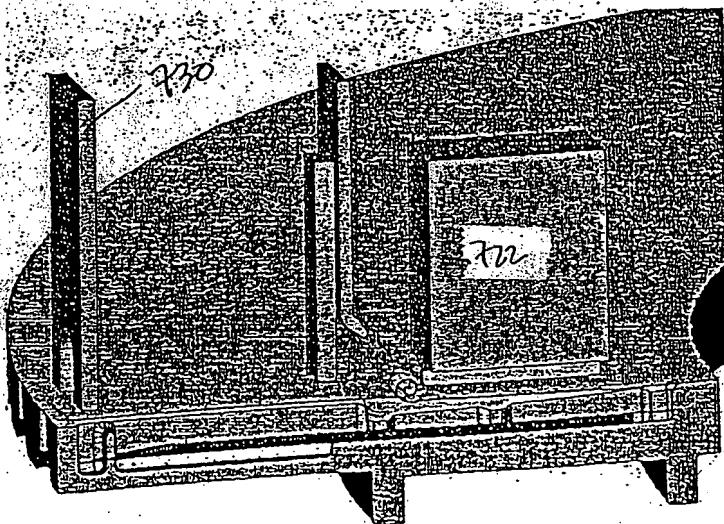


FIG-69L

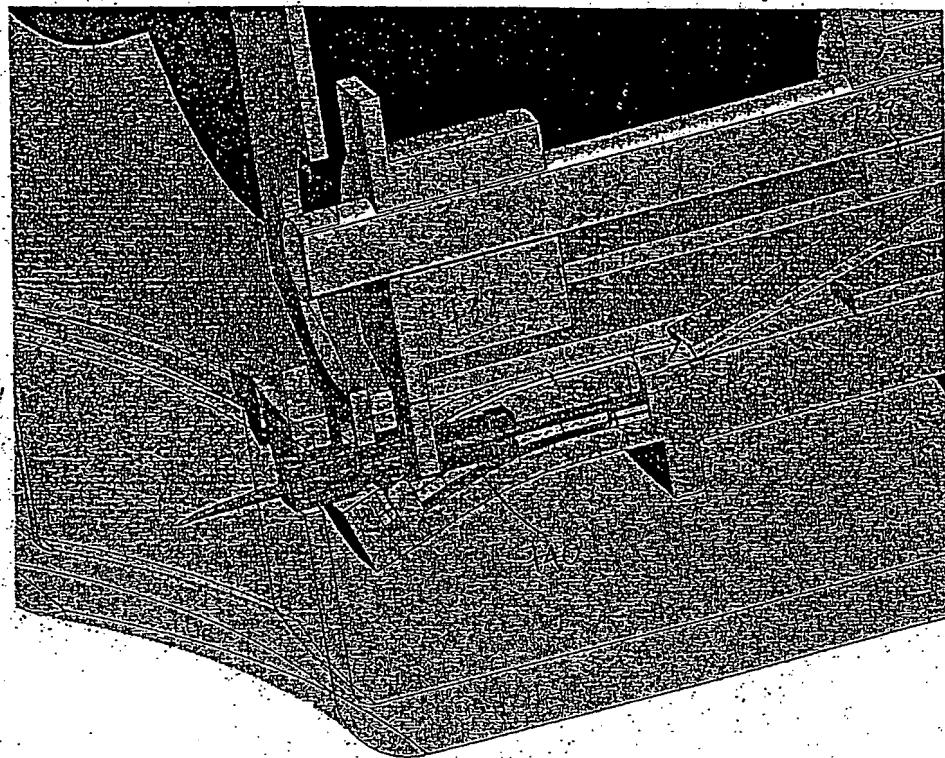


FIG - 70

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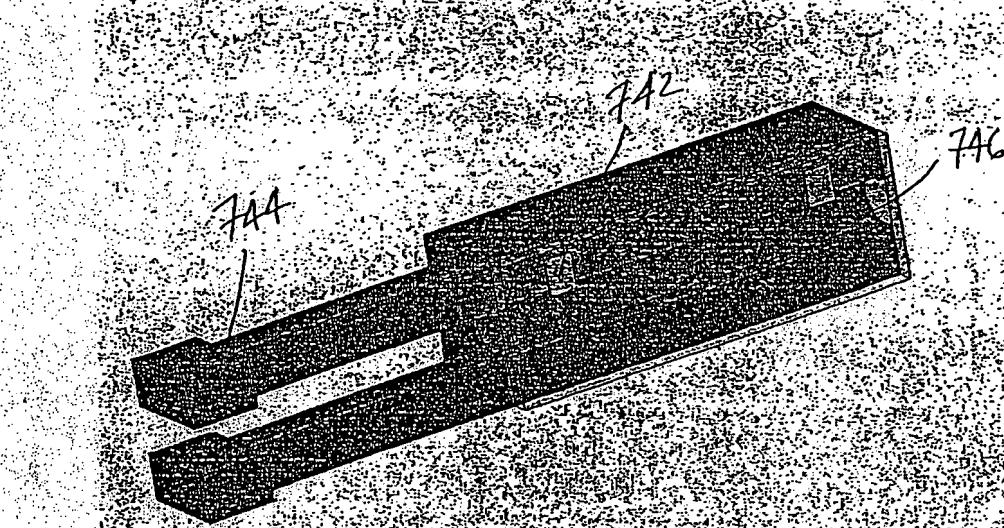


FIG - 71

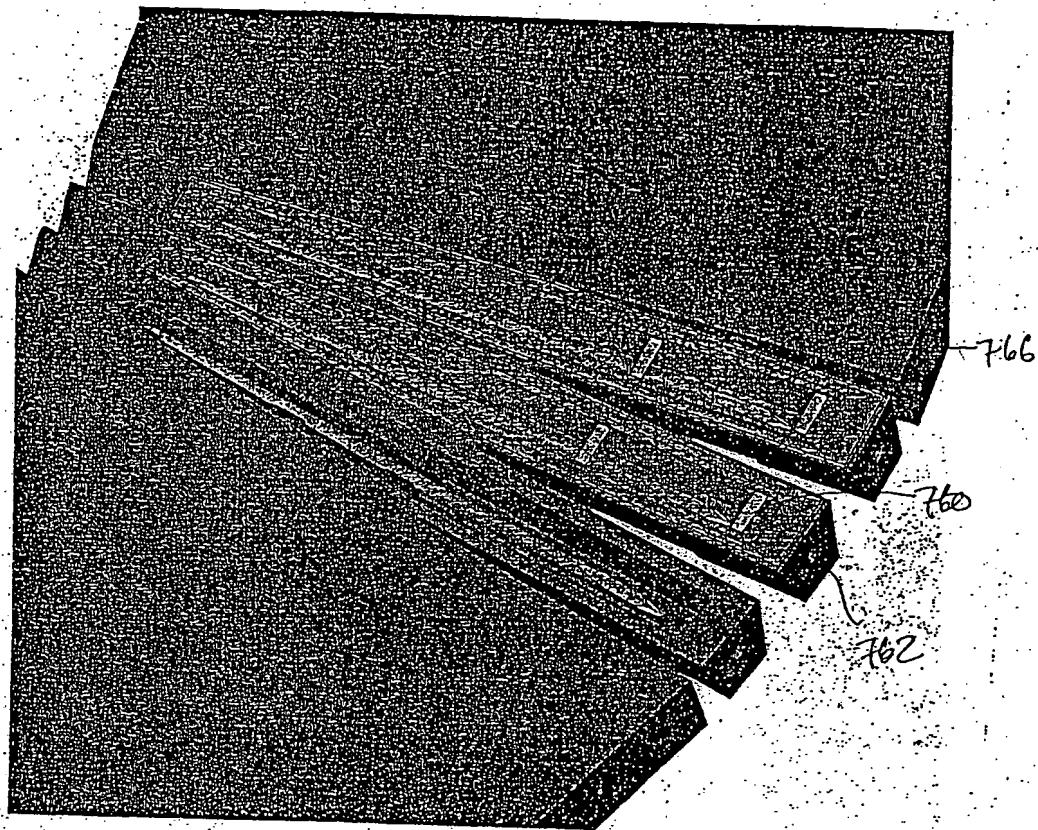
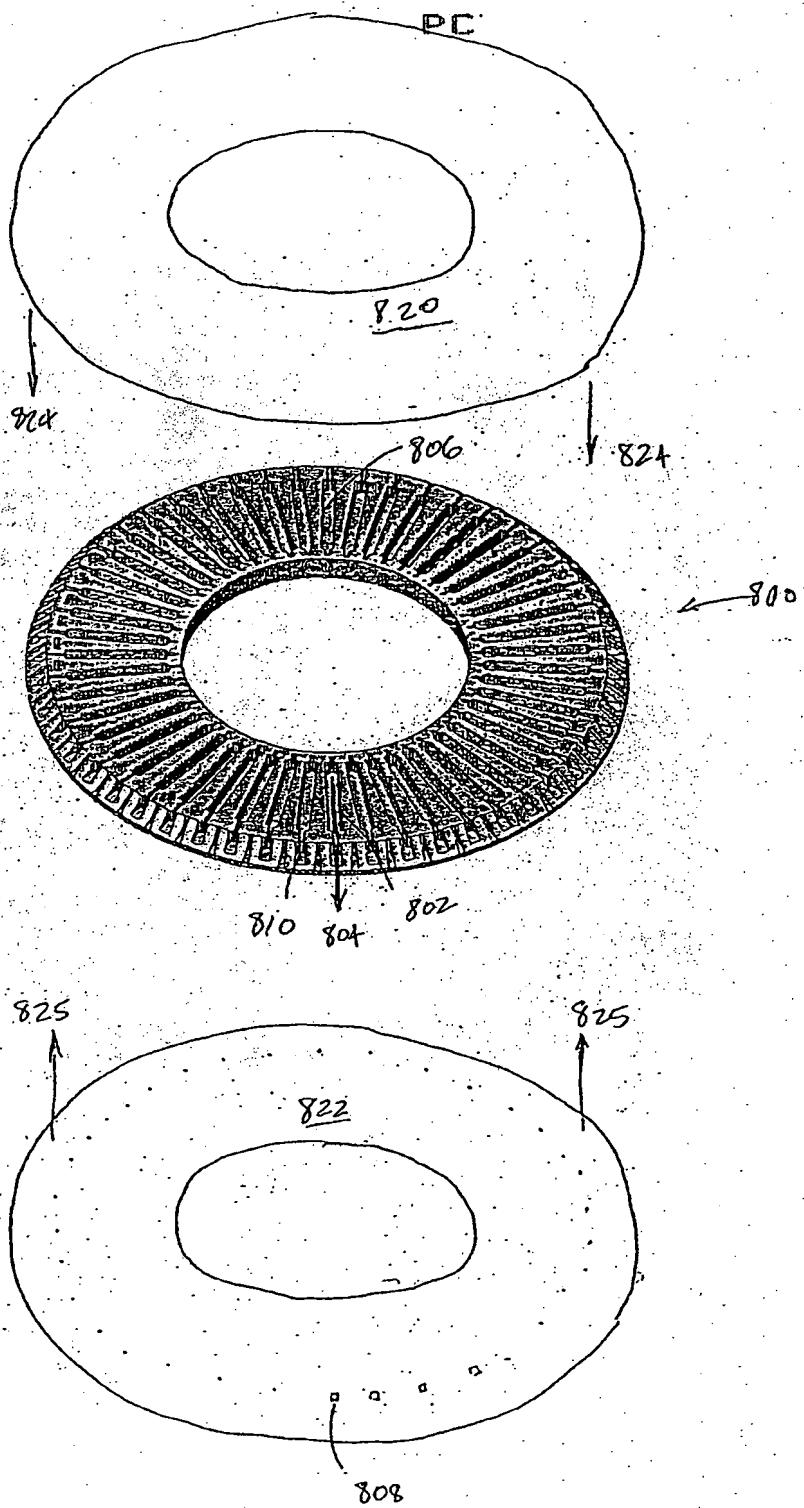


FIG-72

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FIG_73

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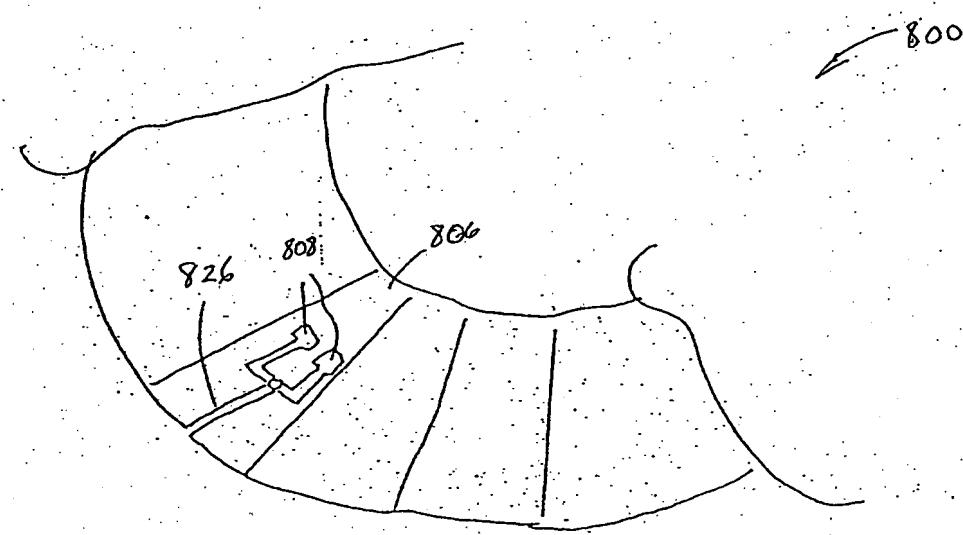


FIG - 74

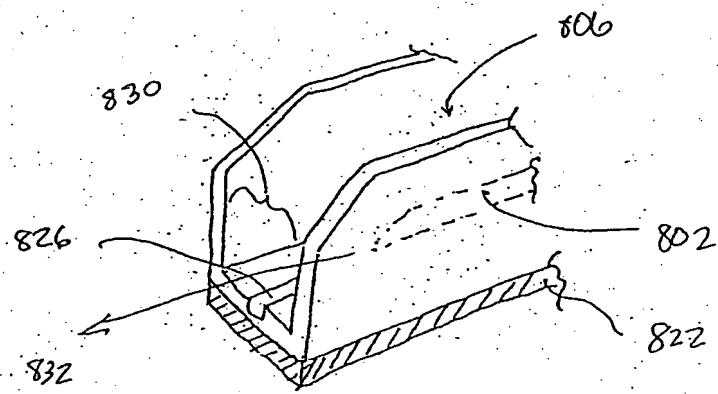


FIG. 75

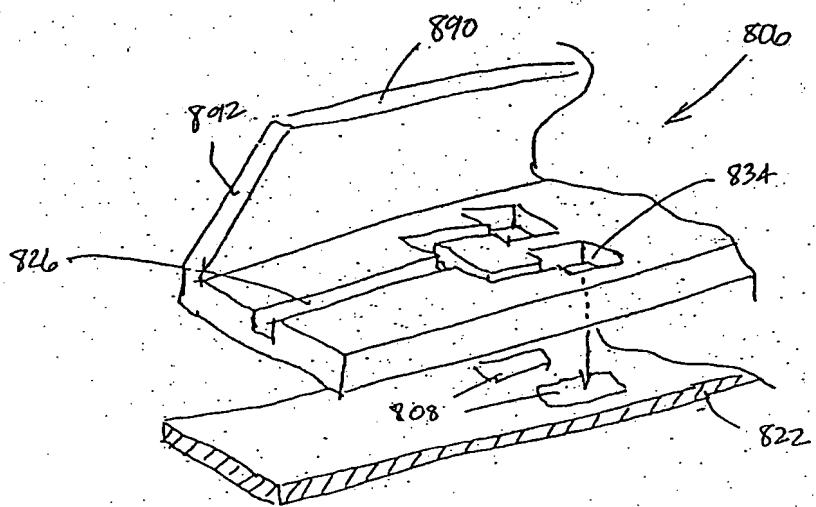
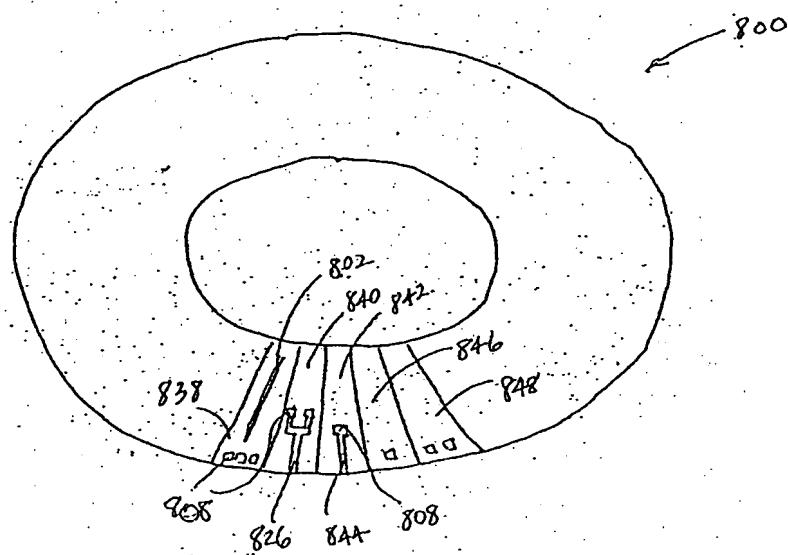


FIG - 76



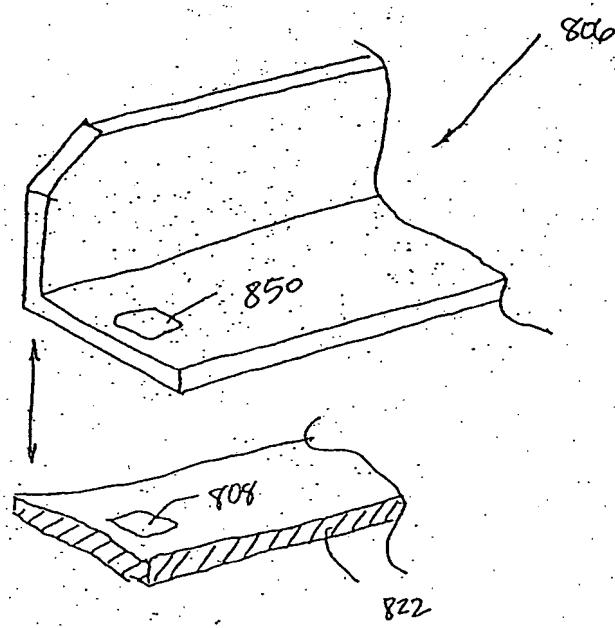


Fig. 78

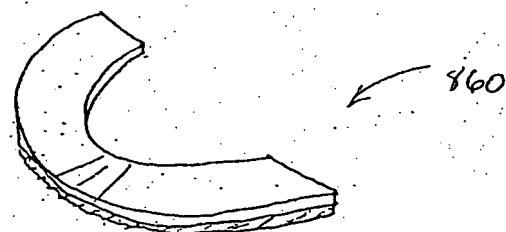


FIG-79

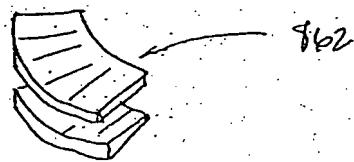


FIG-80

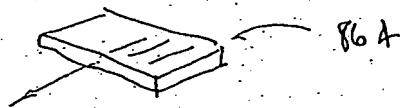


FIG-81

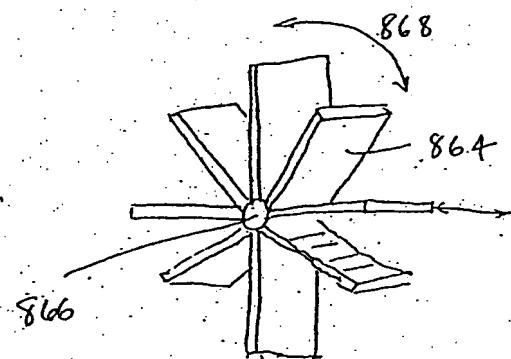


FIG-82

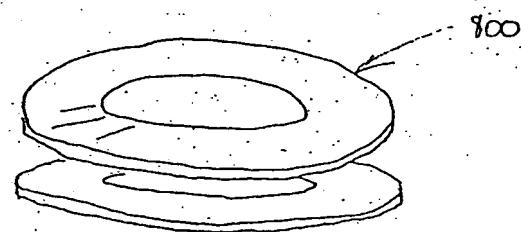


FIG-83

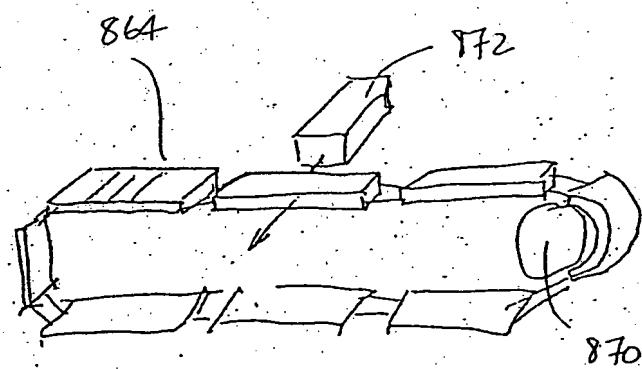
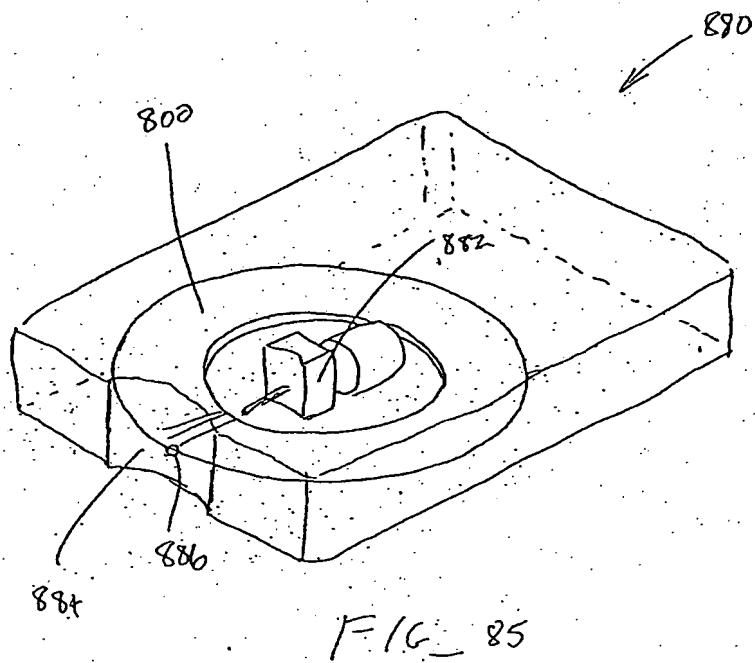


FIG - 84



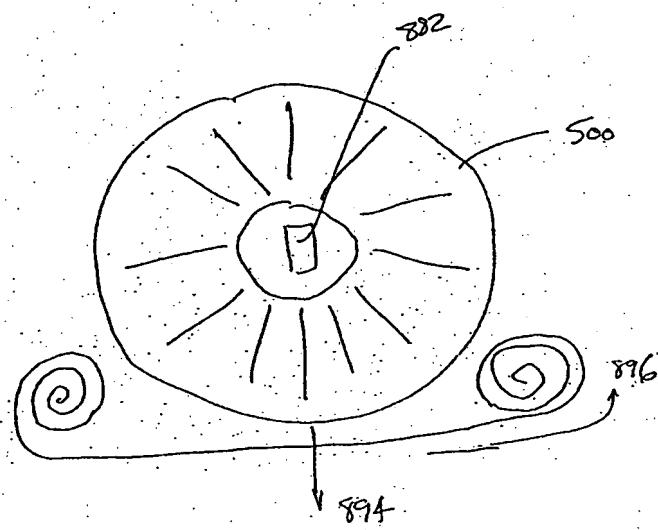
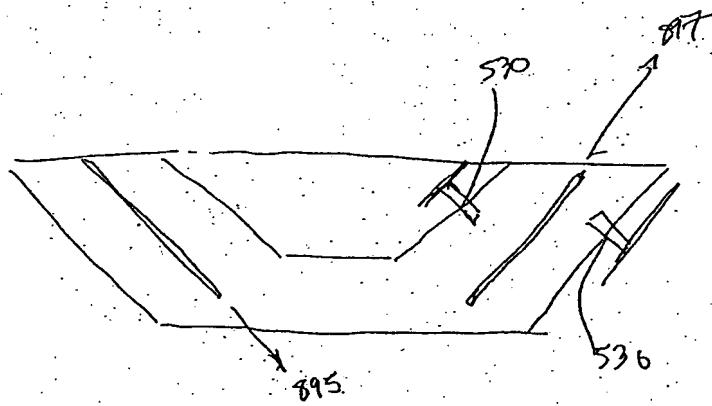


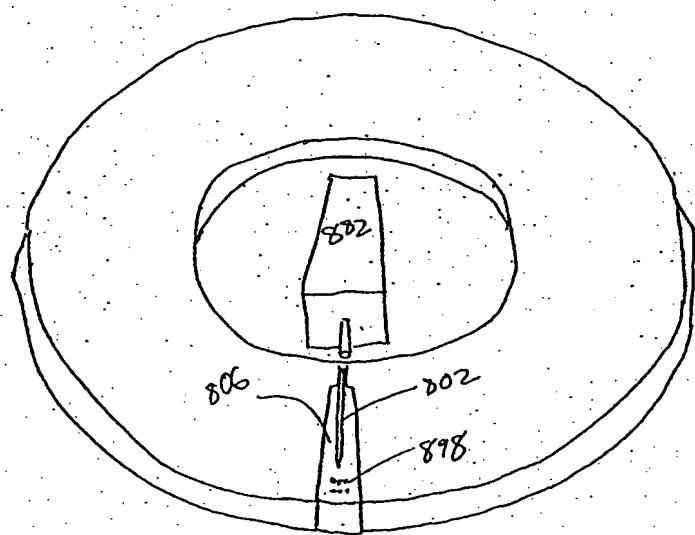
FIG - 86



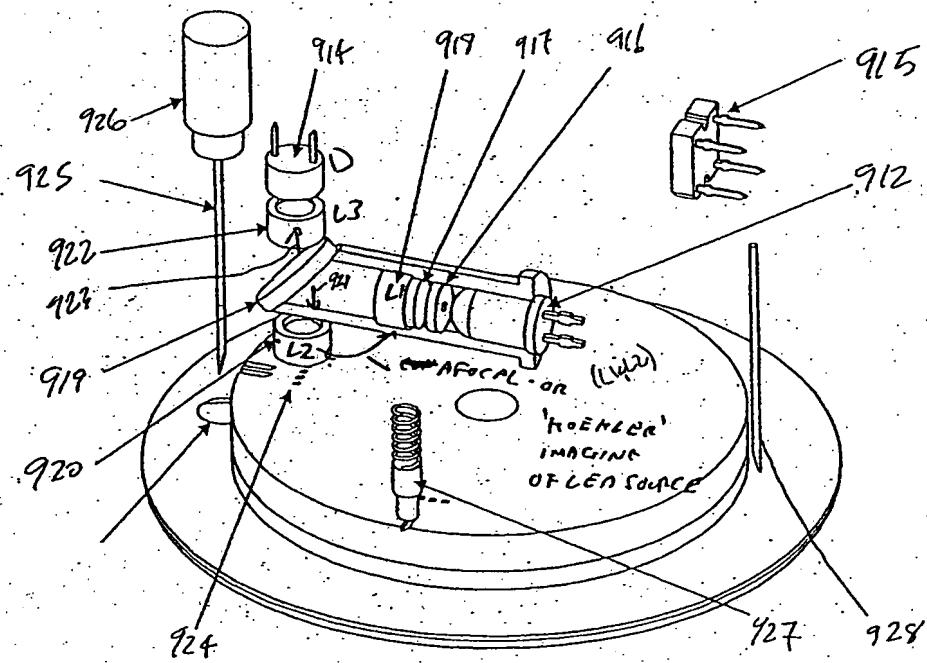
FIG_87A



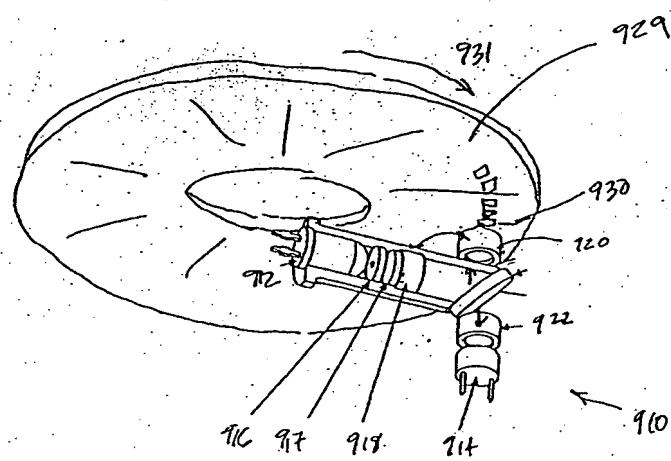
FIG_87B



FIG_ 88



FIG_89



FIG_70

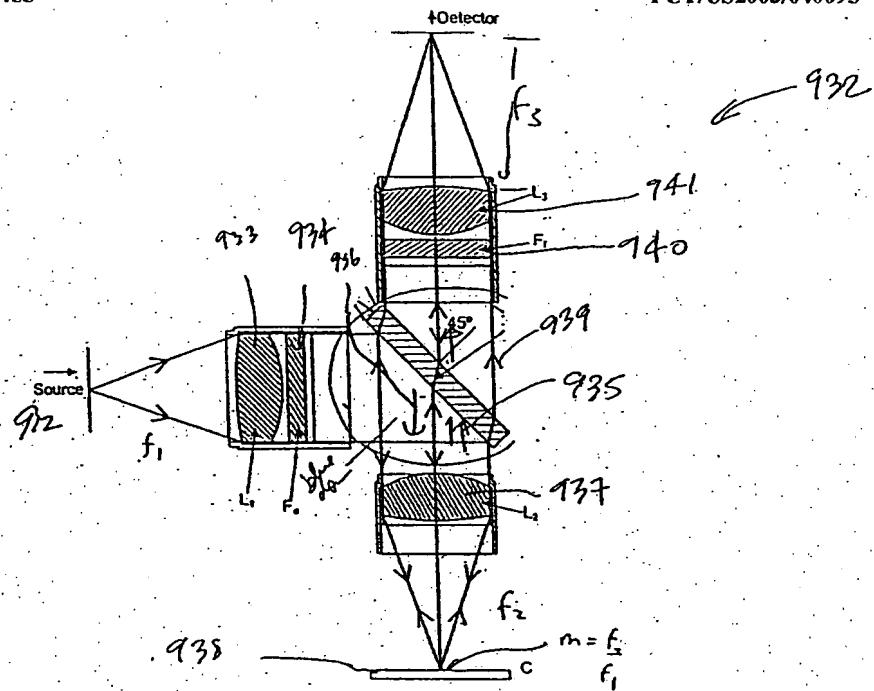


FIG-91

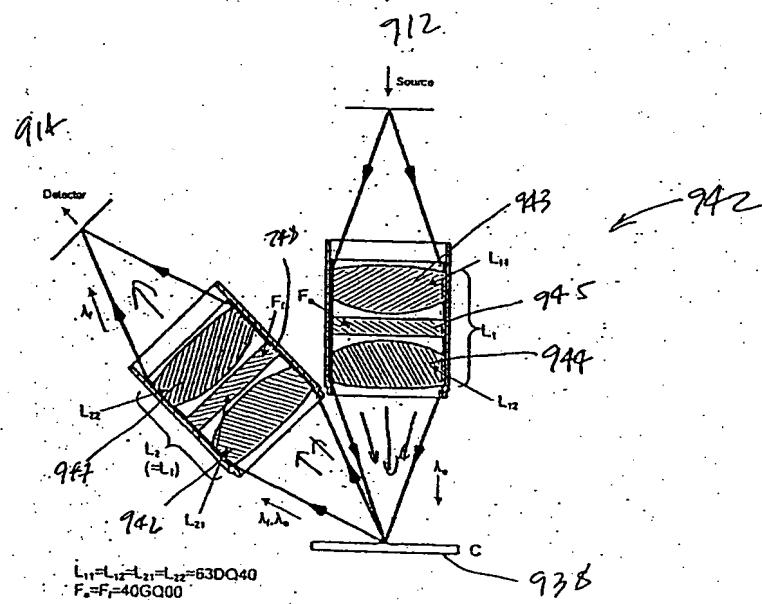
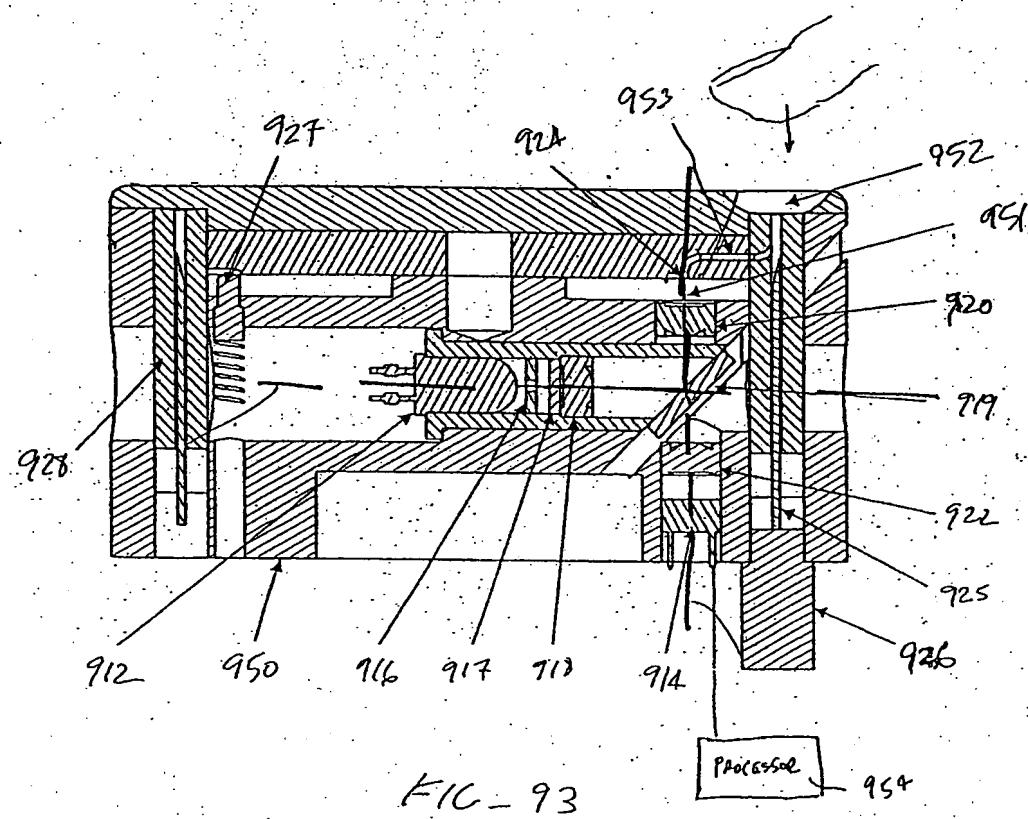


FIG-92



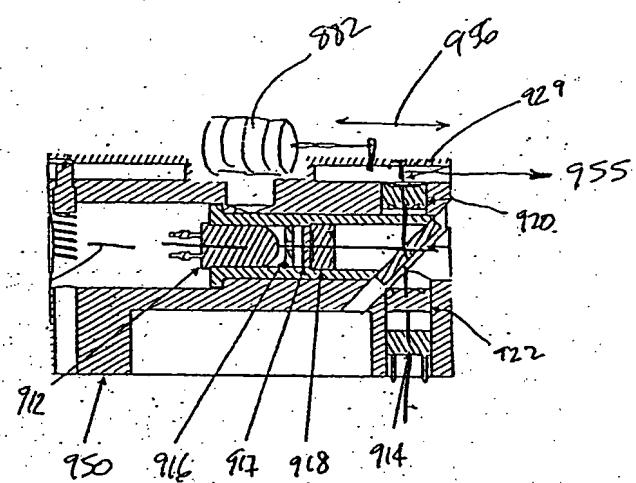


FIG-94

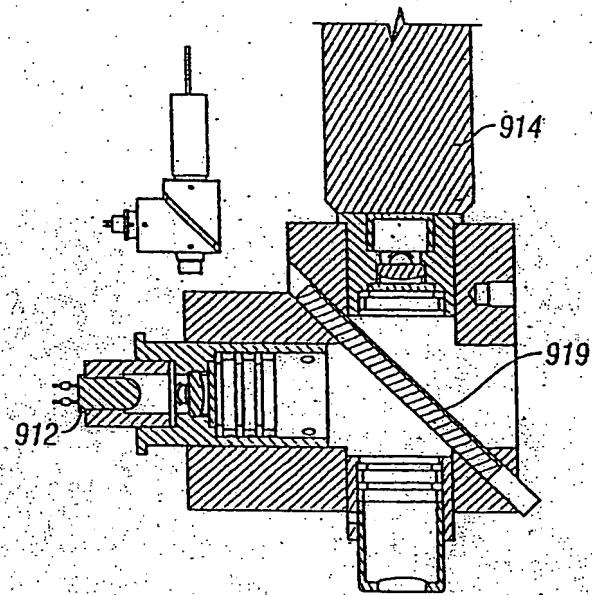


FIG. 95

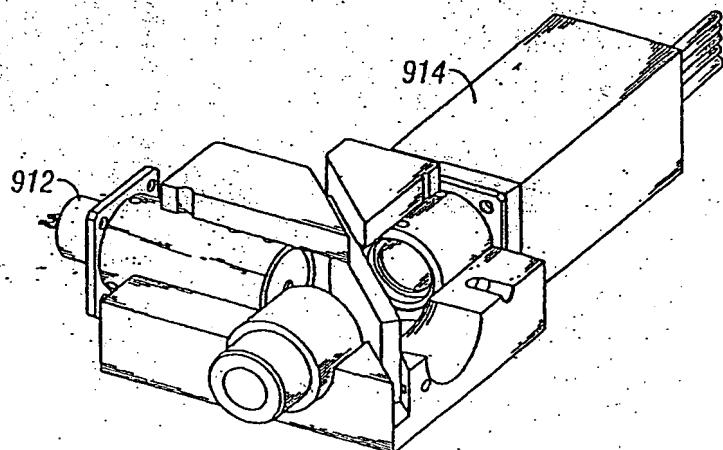


FIG. 96

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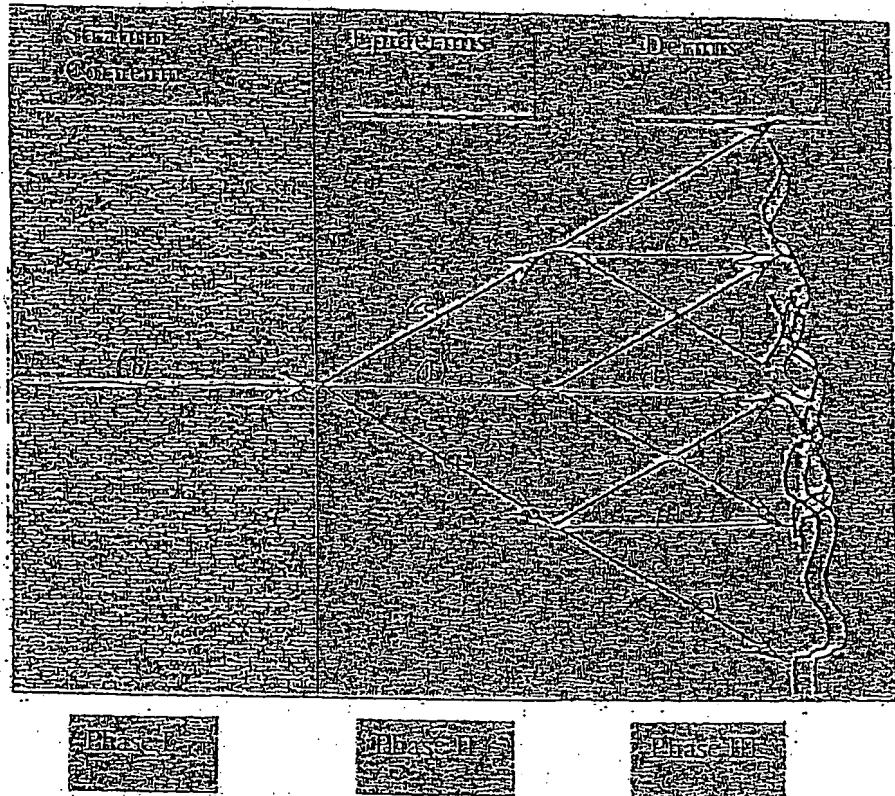
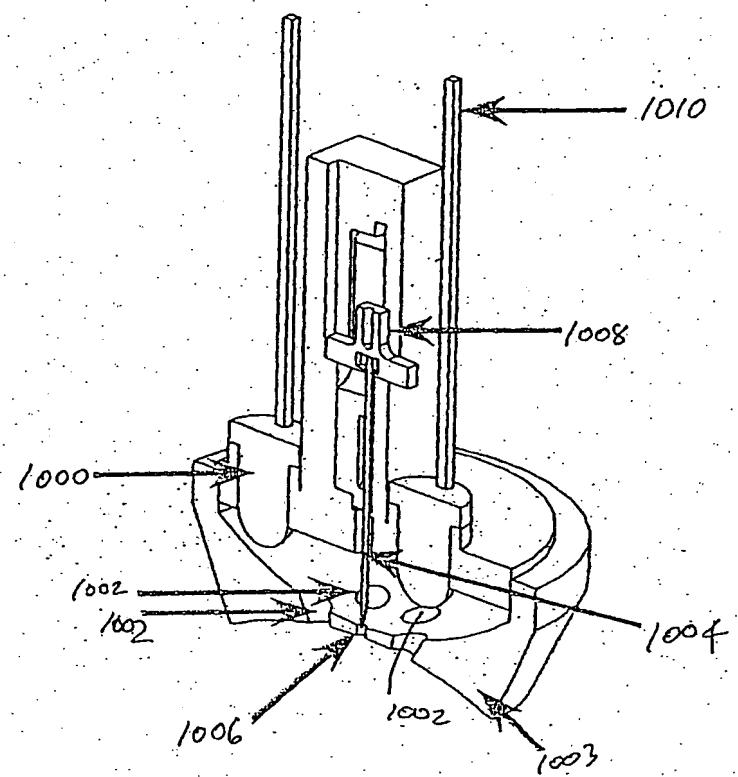


FIG. 97



FIG_78

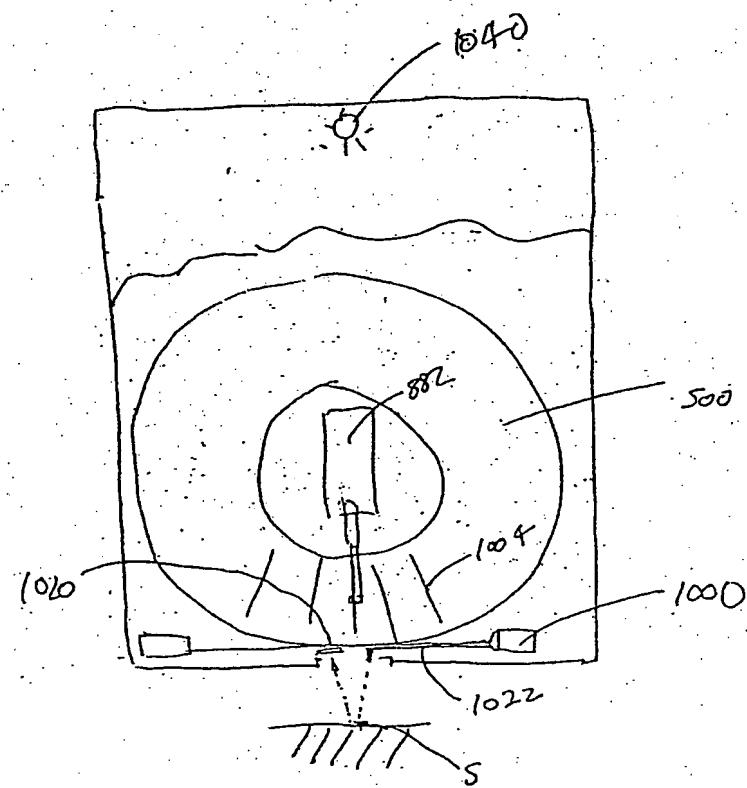


FIG - 99

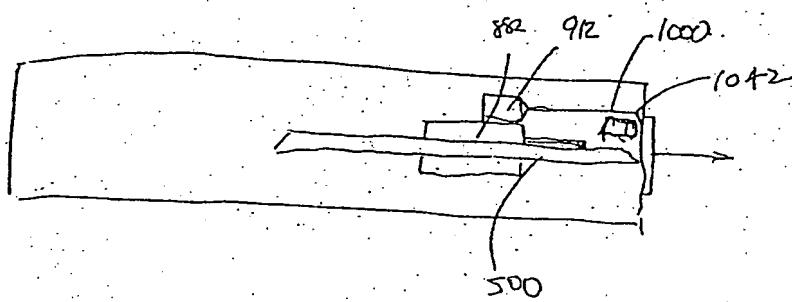
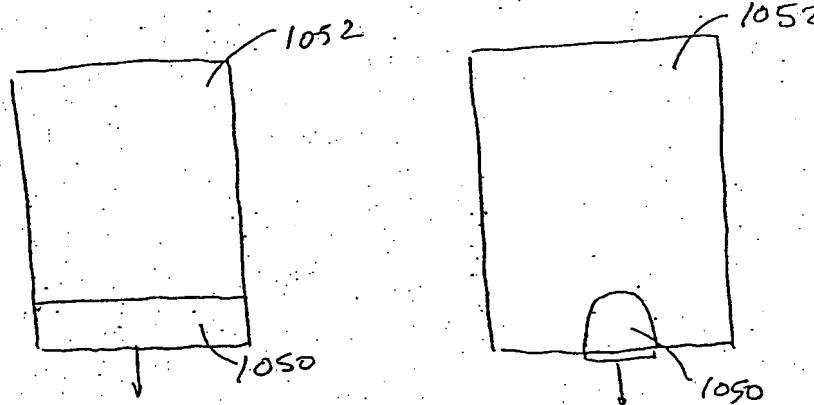


FIG - 100.



FIG_101

FIG_102

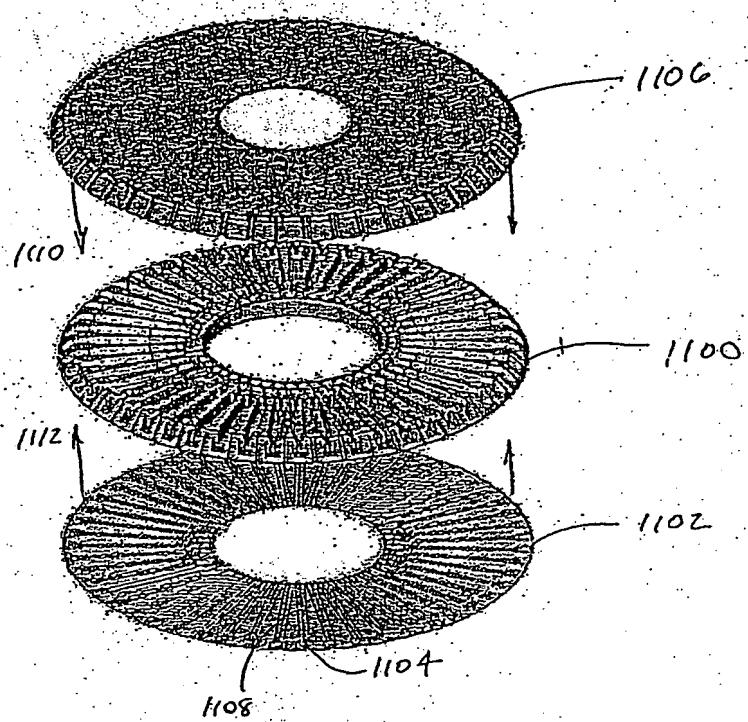


FIG-103

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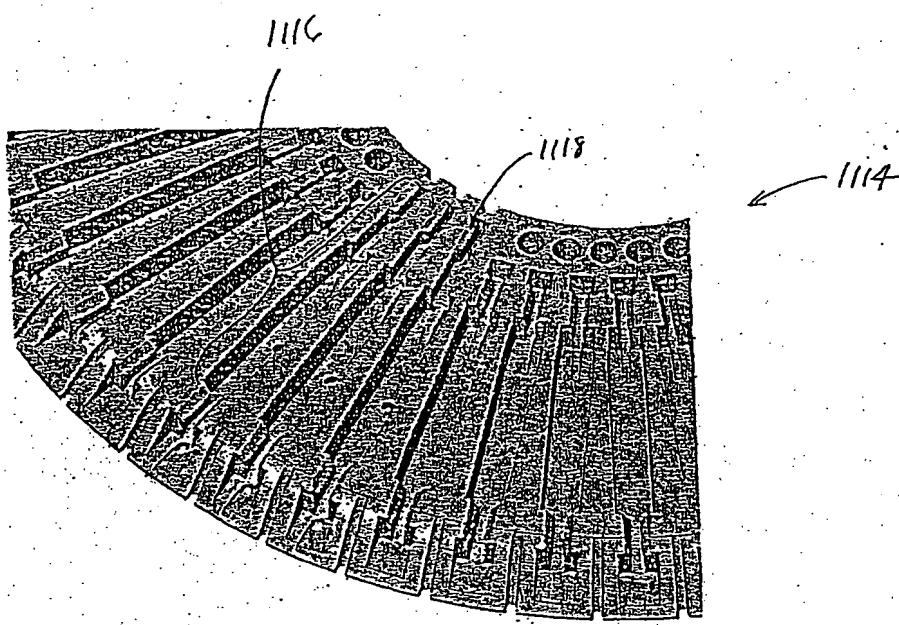


FIG-104

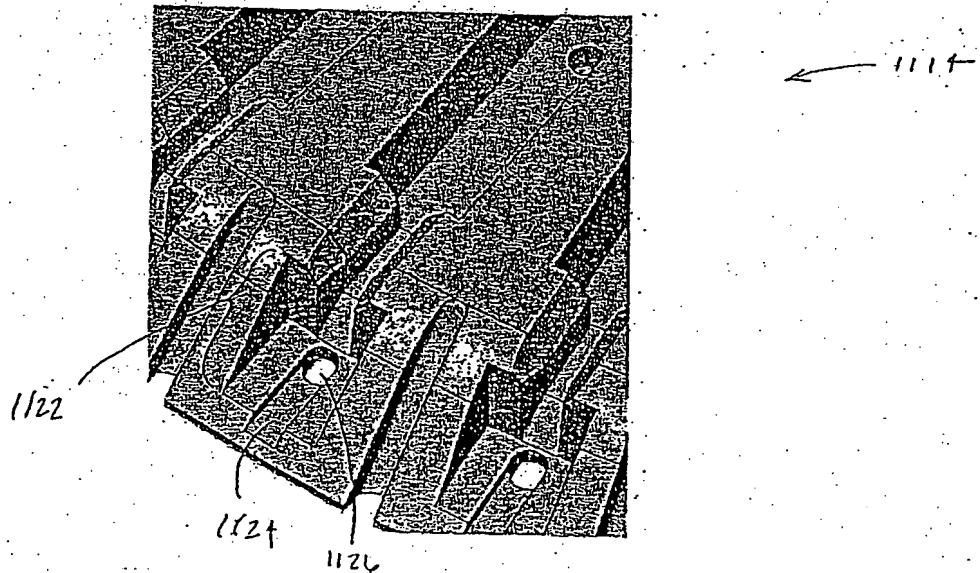


FIG-105

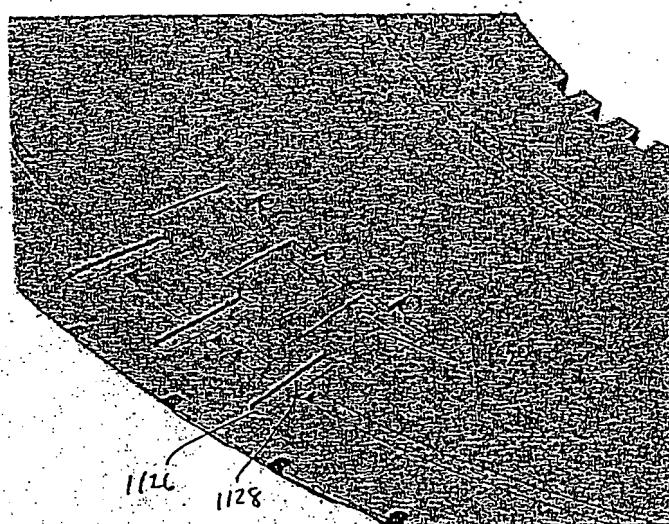


FIG - 106

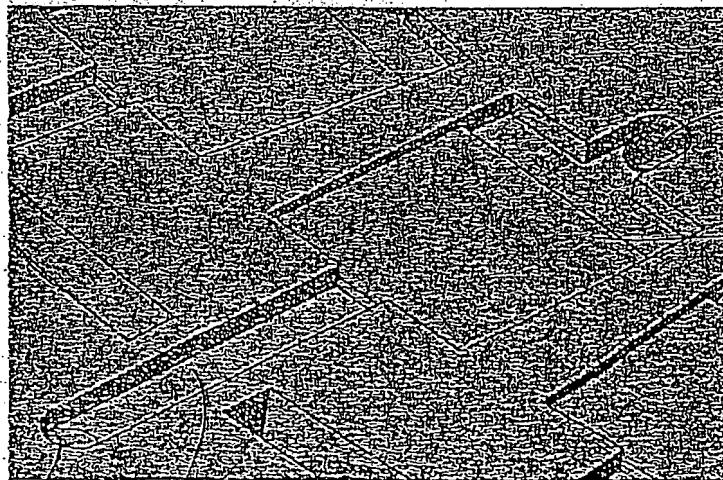


FIG - 107

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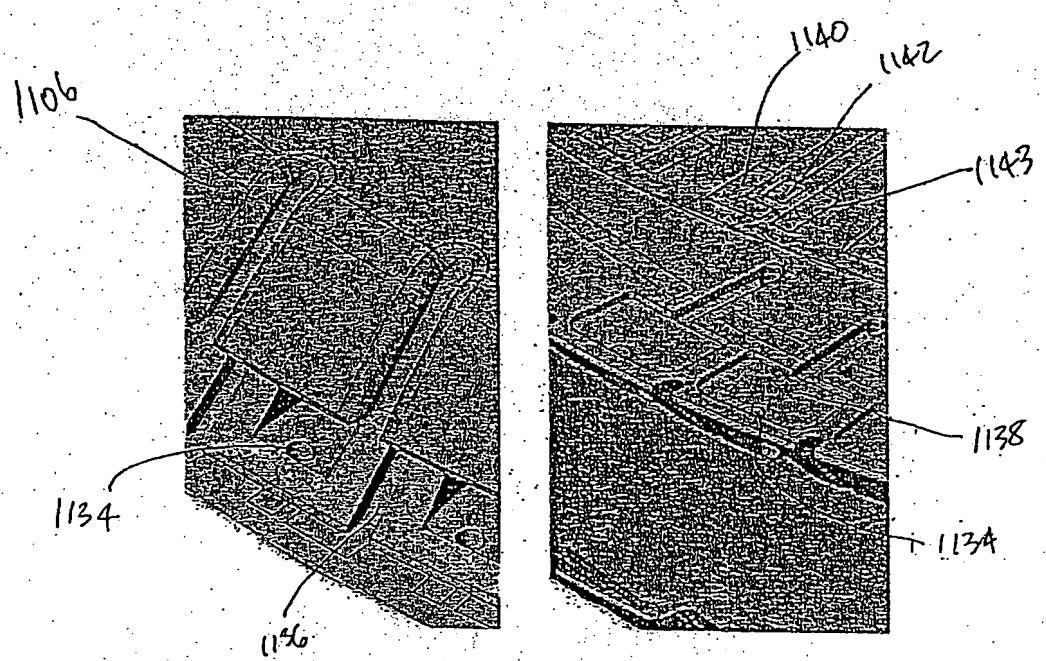
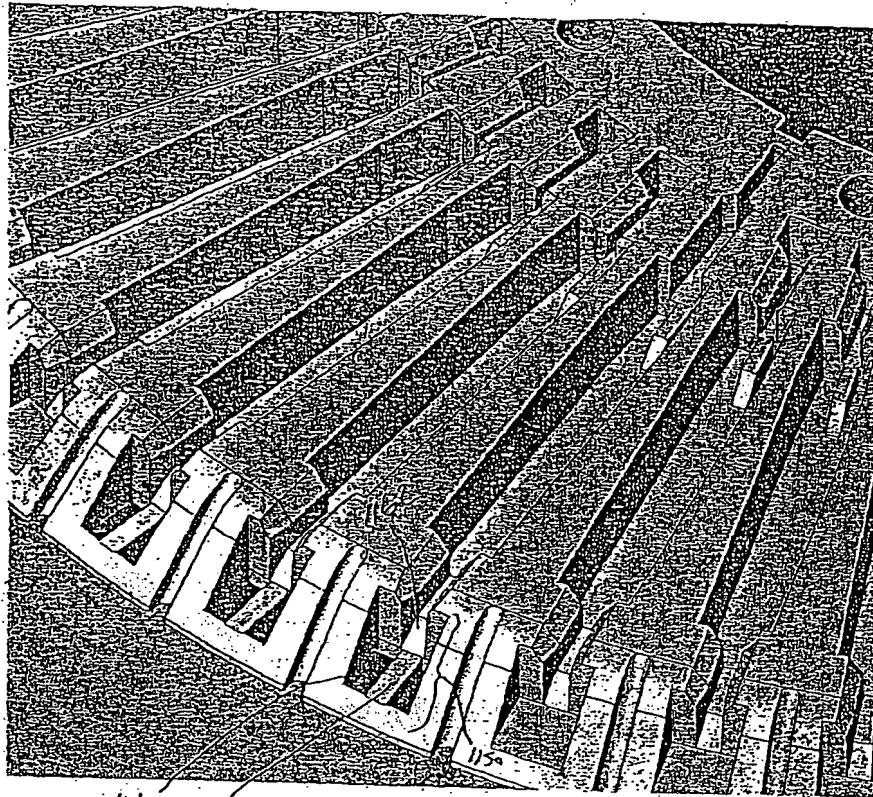


FIG - 108

FIG - 109

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1148 1146 FIG - 110
1150

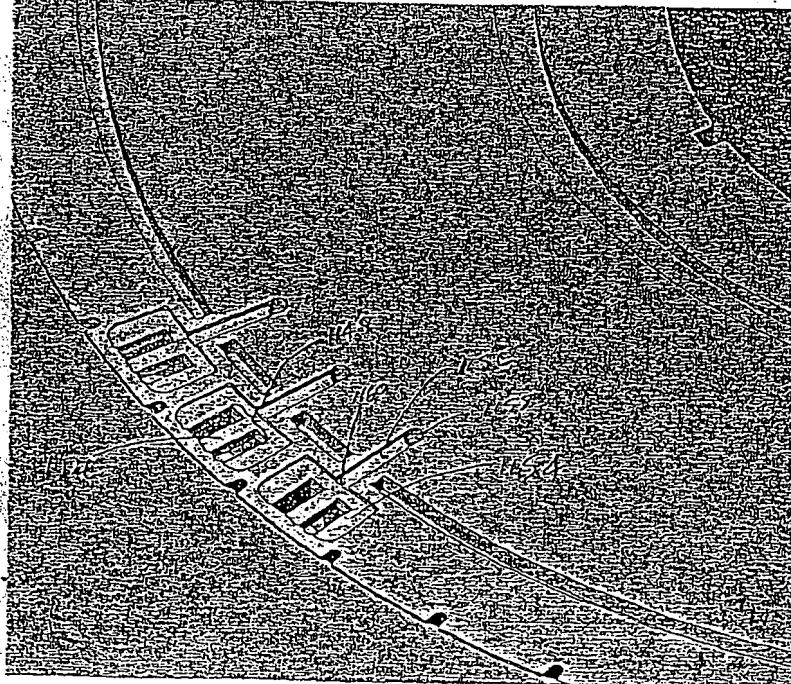


FIG - 11
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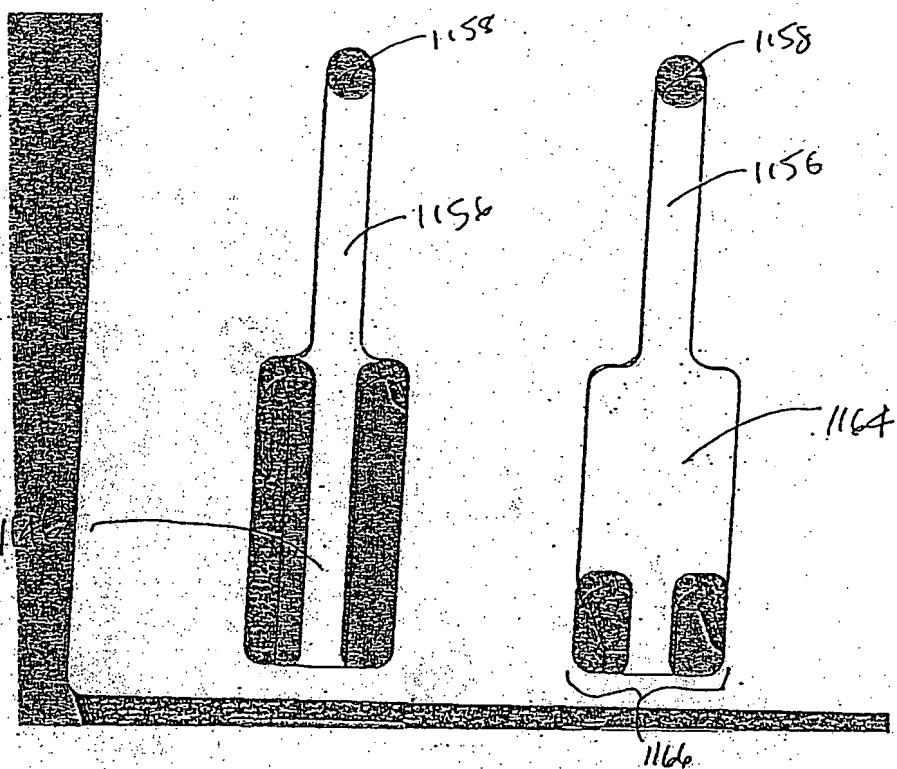


FIG-112

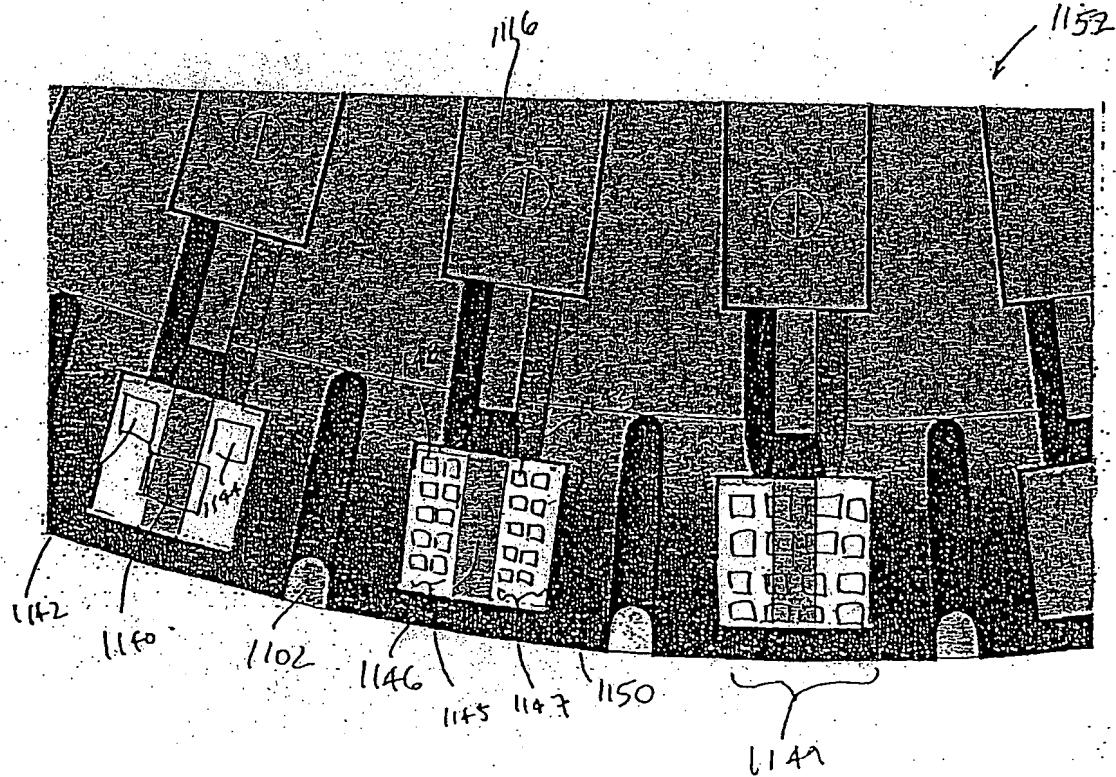


FIG-113

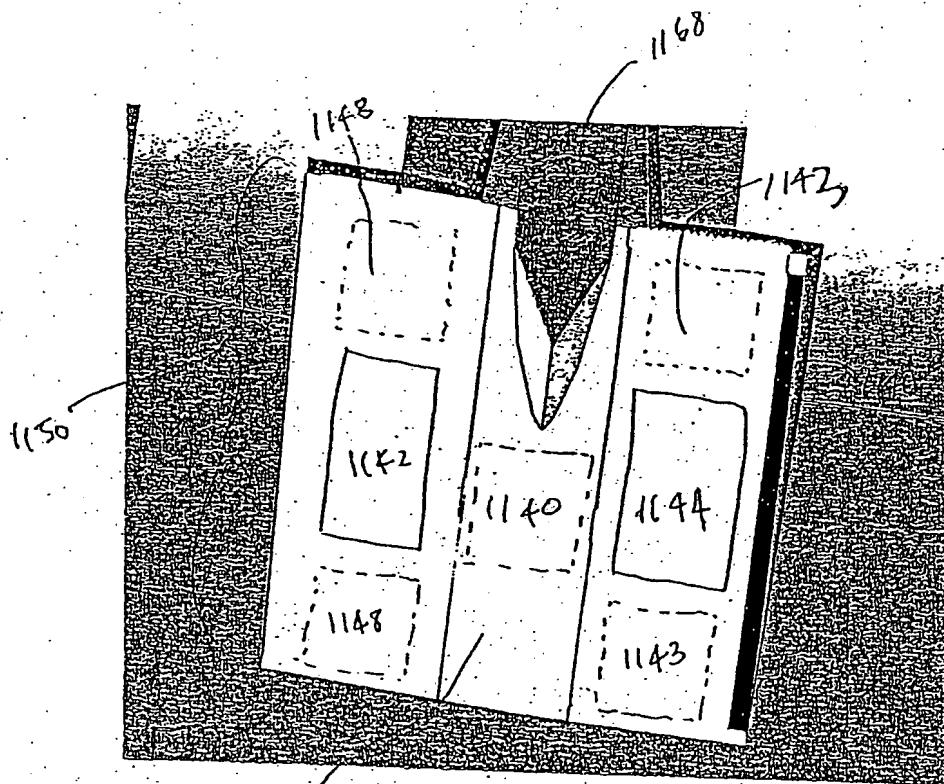


FIG-114

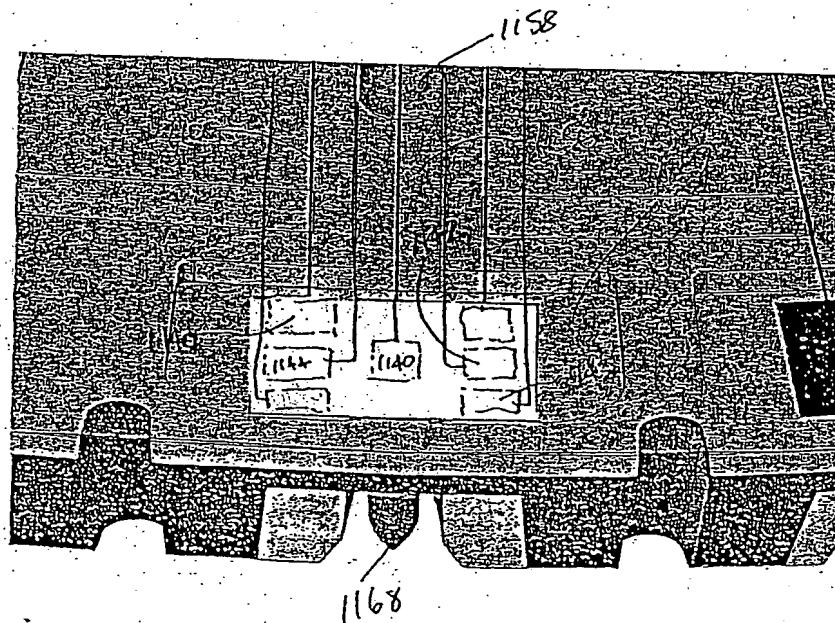


FIG-115

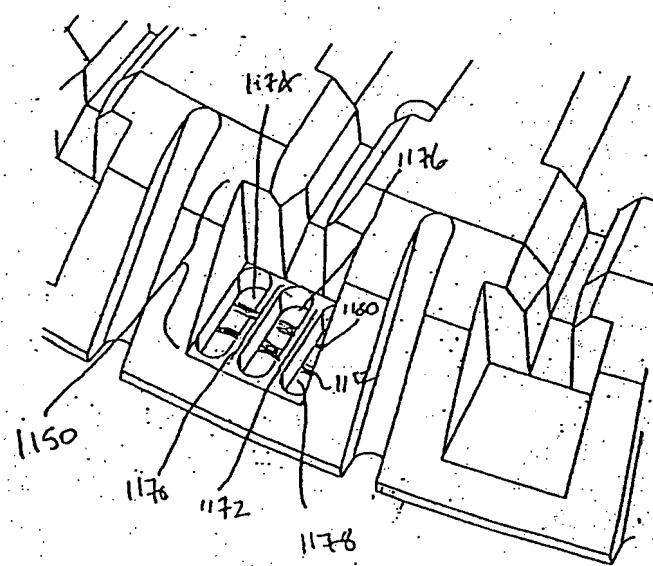


FIG-116

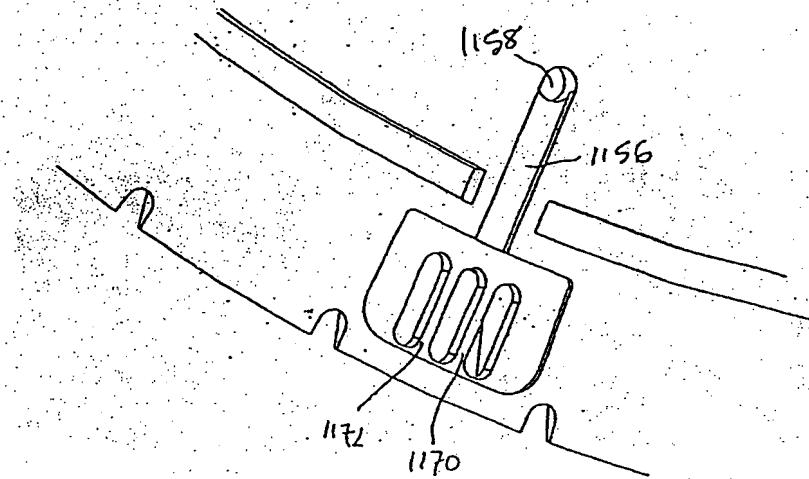


FIG-117

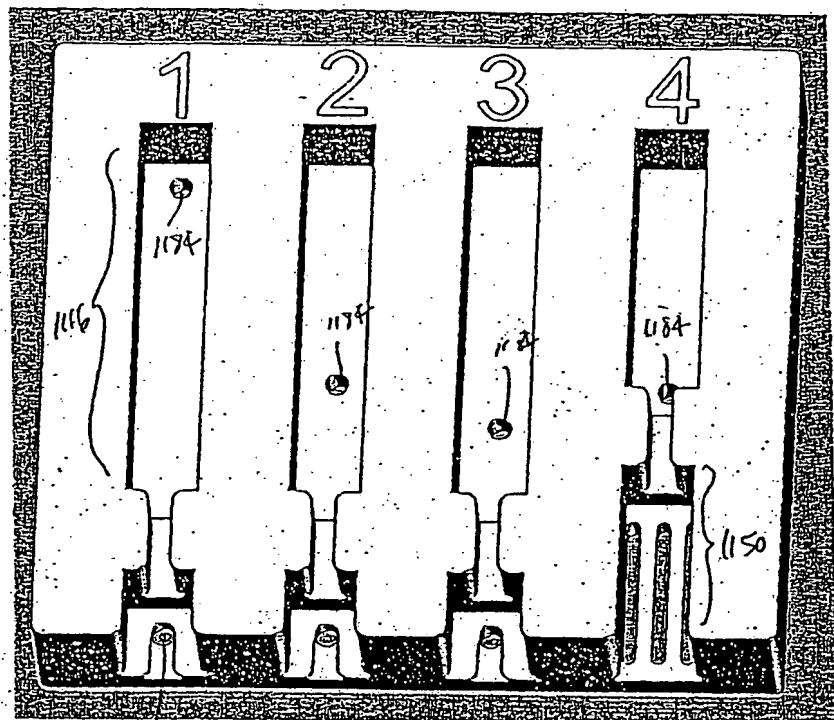


FIG - 118

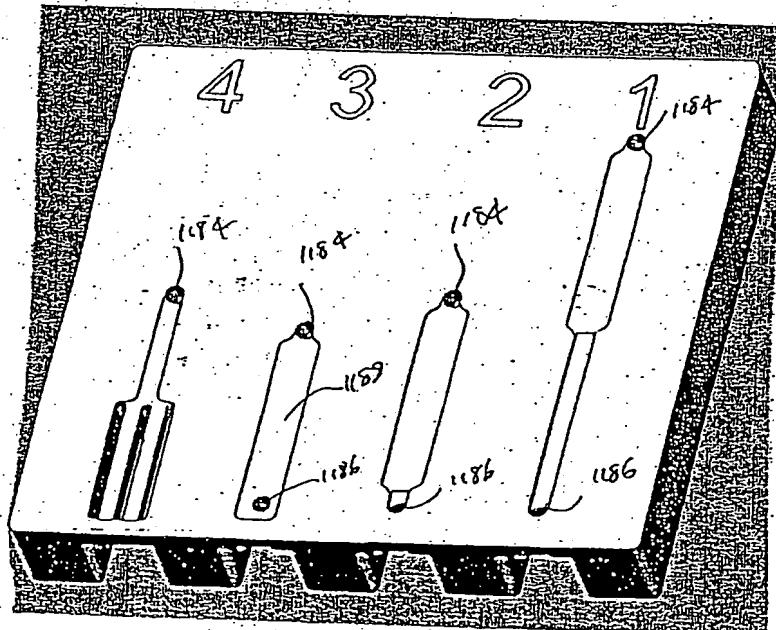


FIG - 119

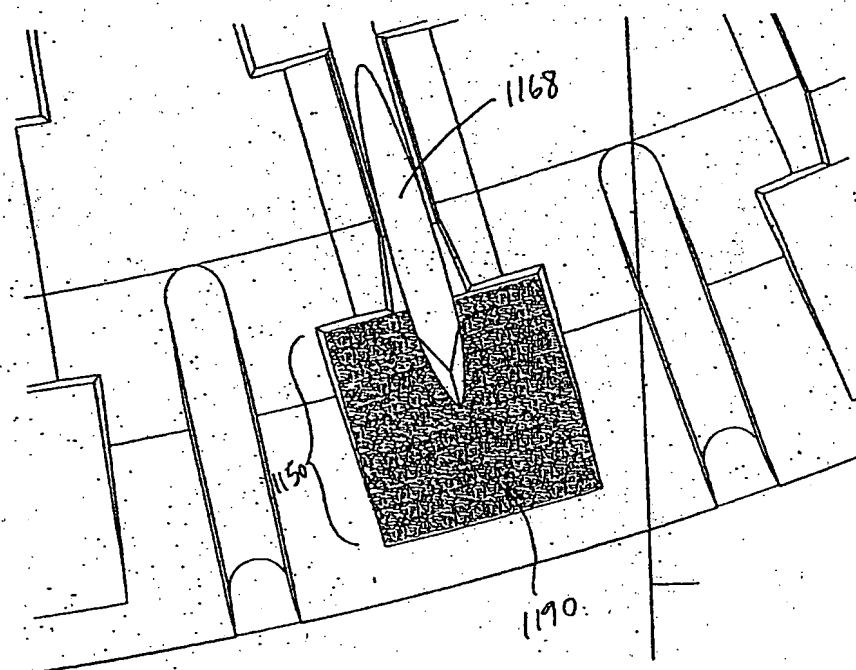


FIG - 120

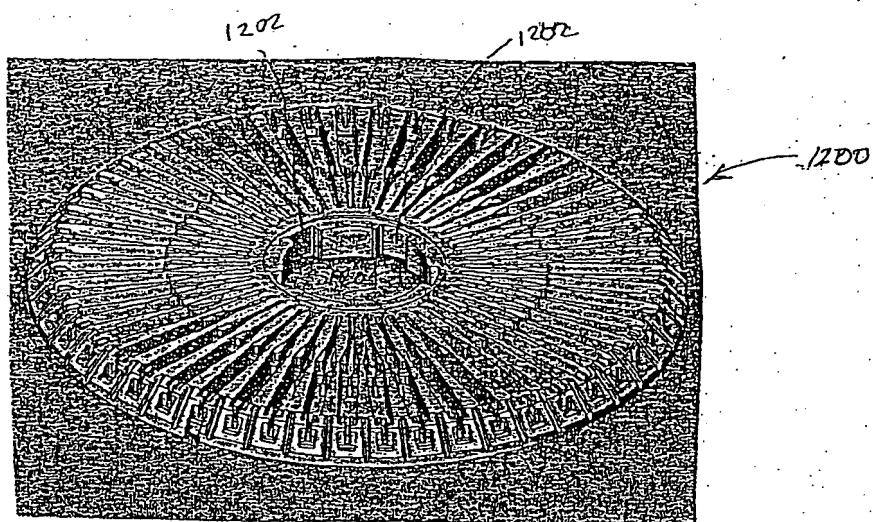


FIG-121

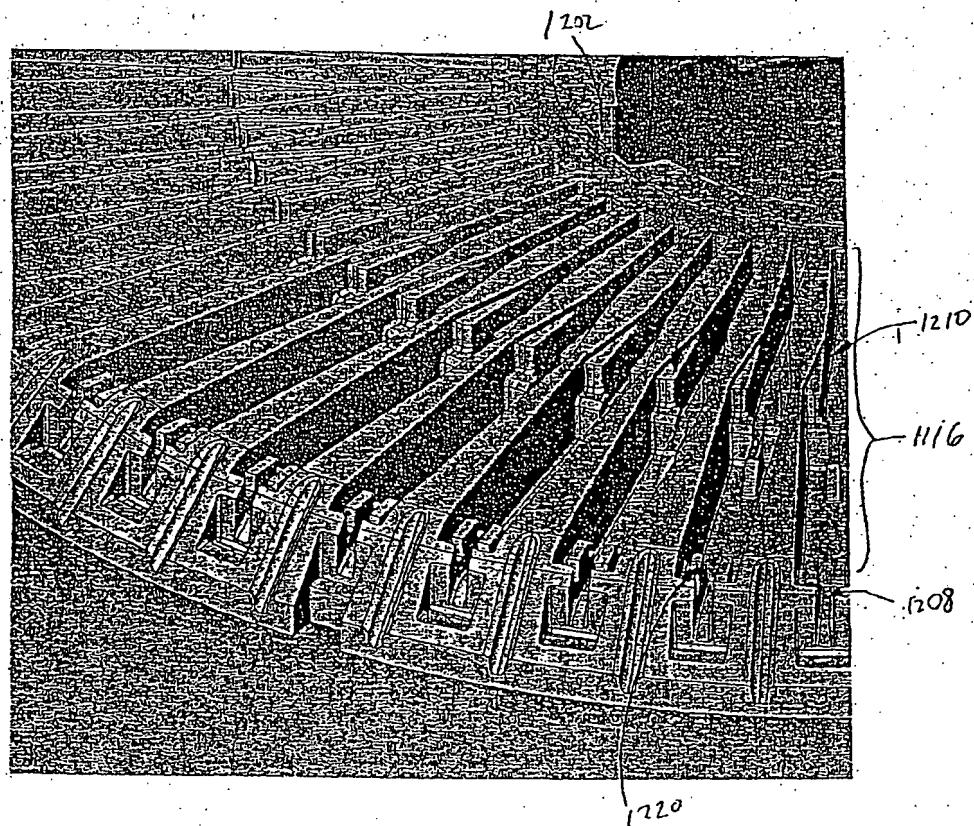


FIG-122.

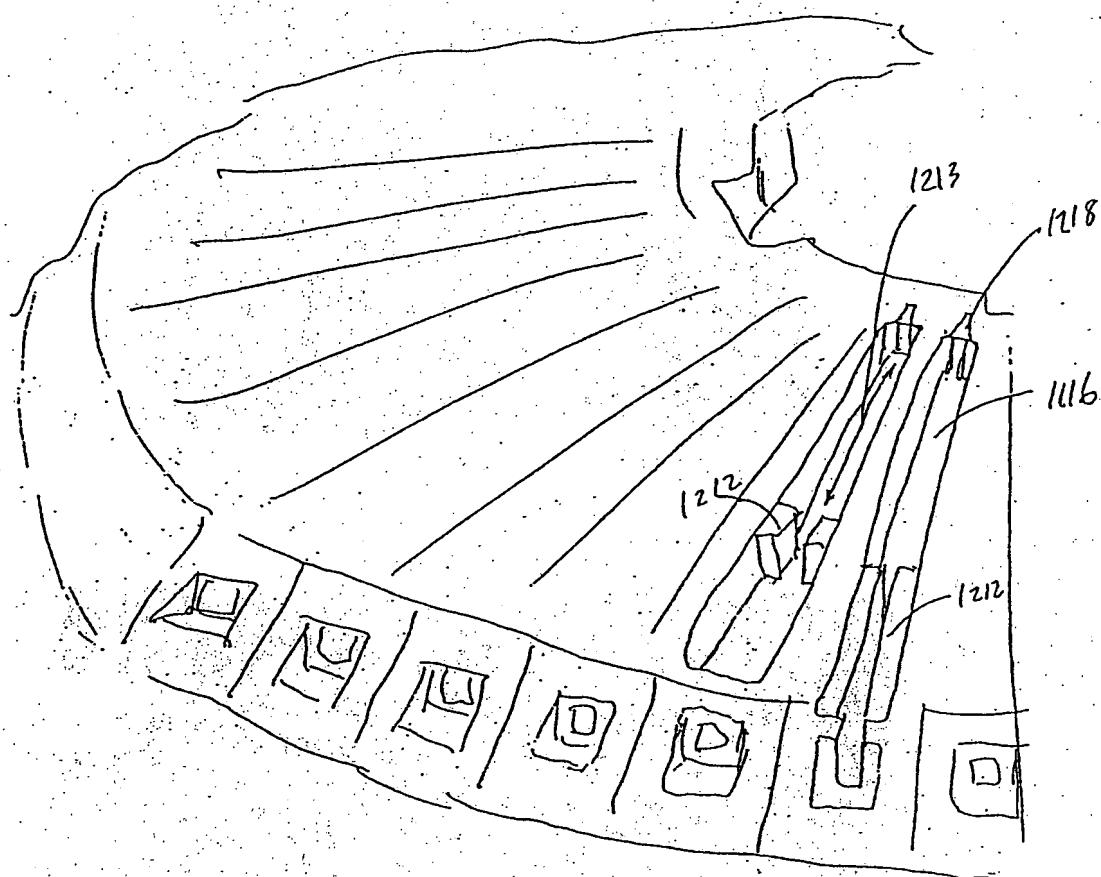


FIG-123

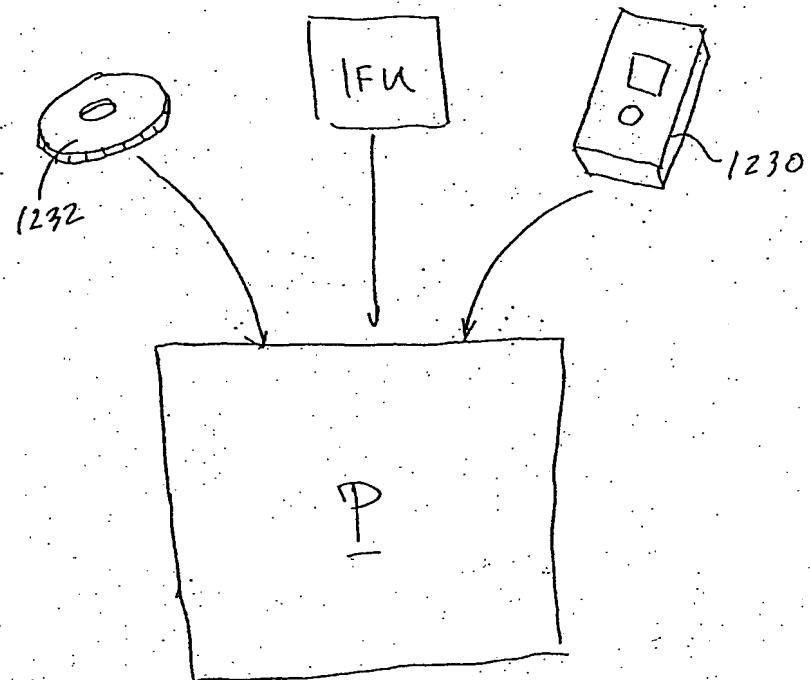


FIG-124

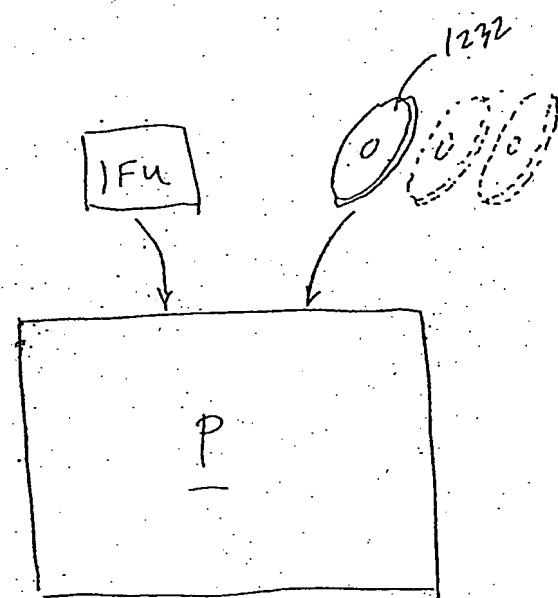


FIG-125

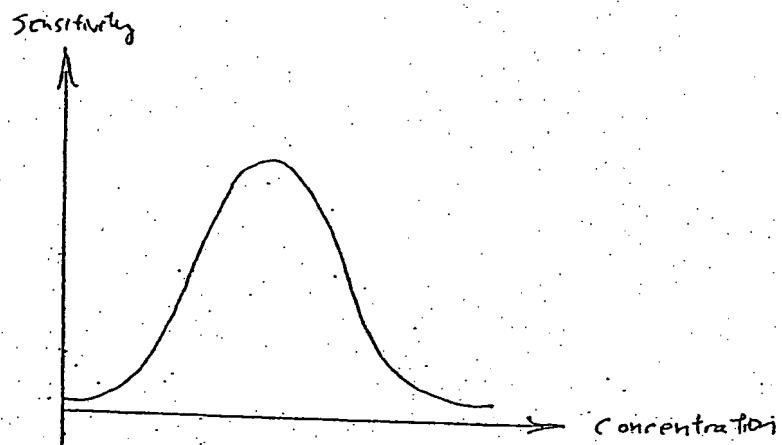


FIG - 126

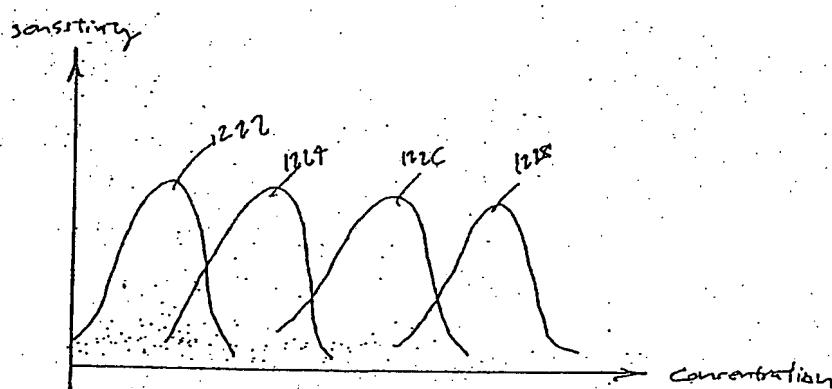


FIG - 127

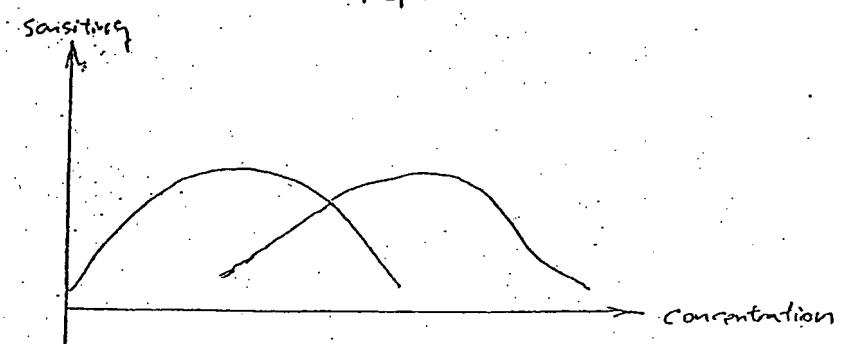


FIG - 128

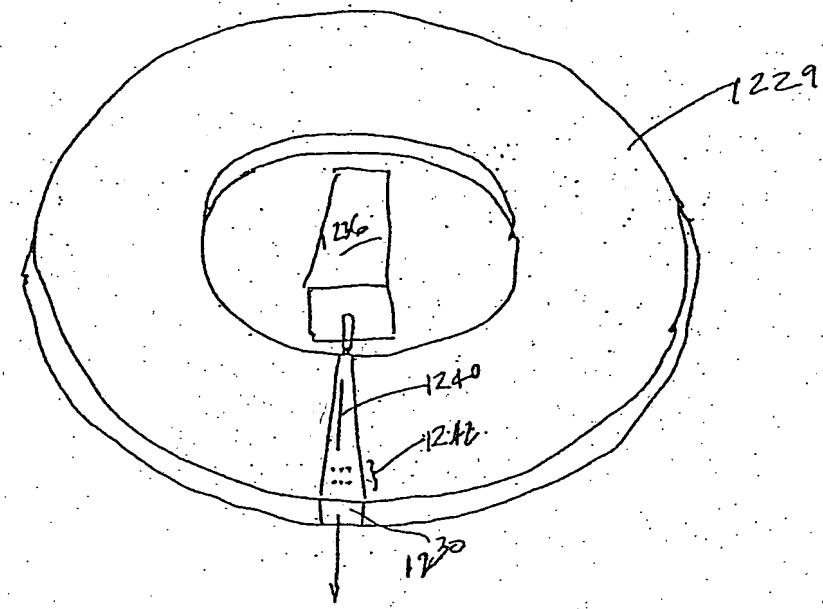
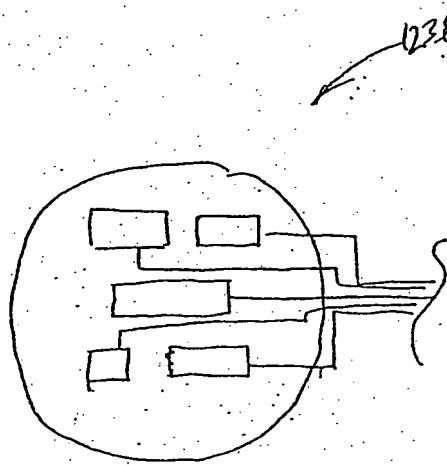


FIG - 129

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FIG_130

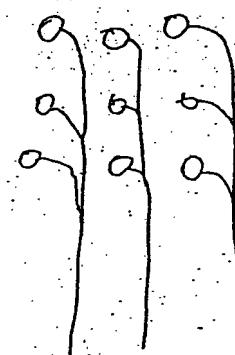


FIG-131

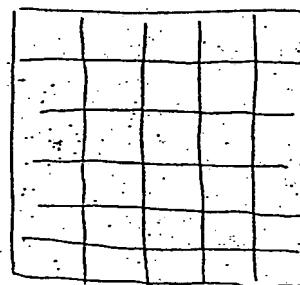
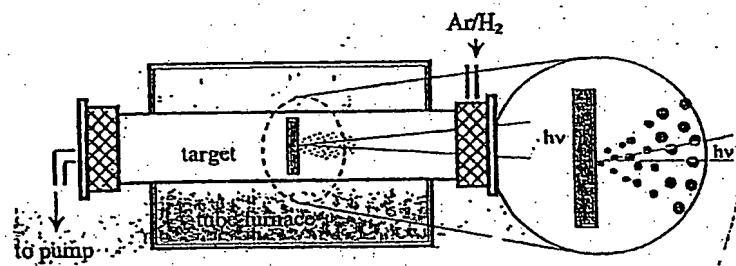
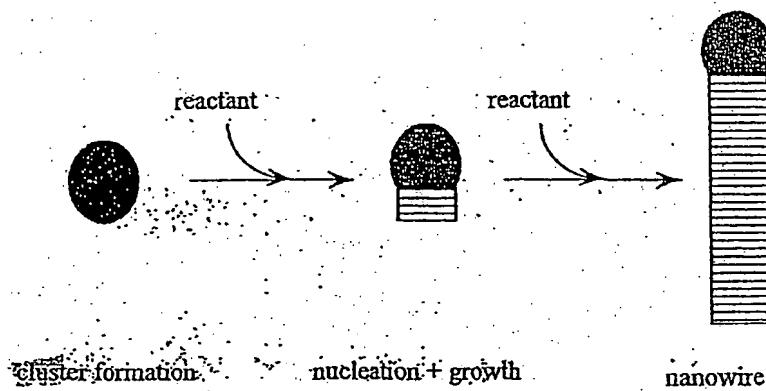


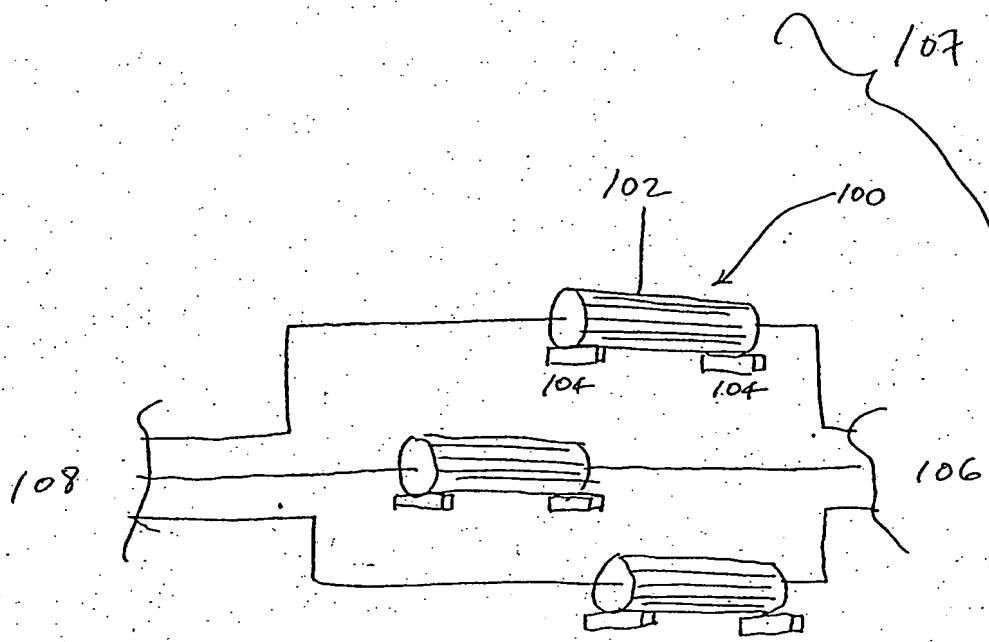
FIG-132



FIG_133A



FIG_133B



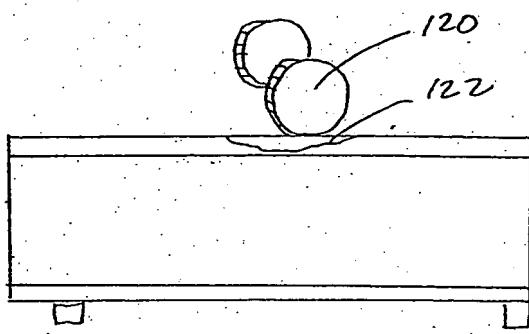


FIG-135

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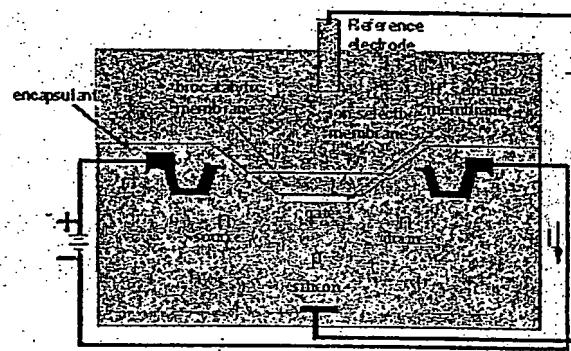


FIG - 136.

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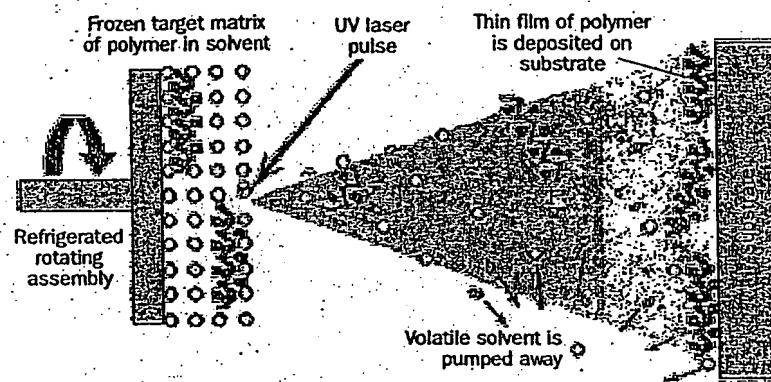
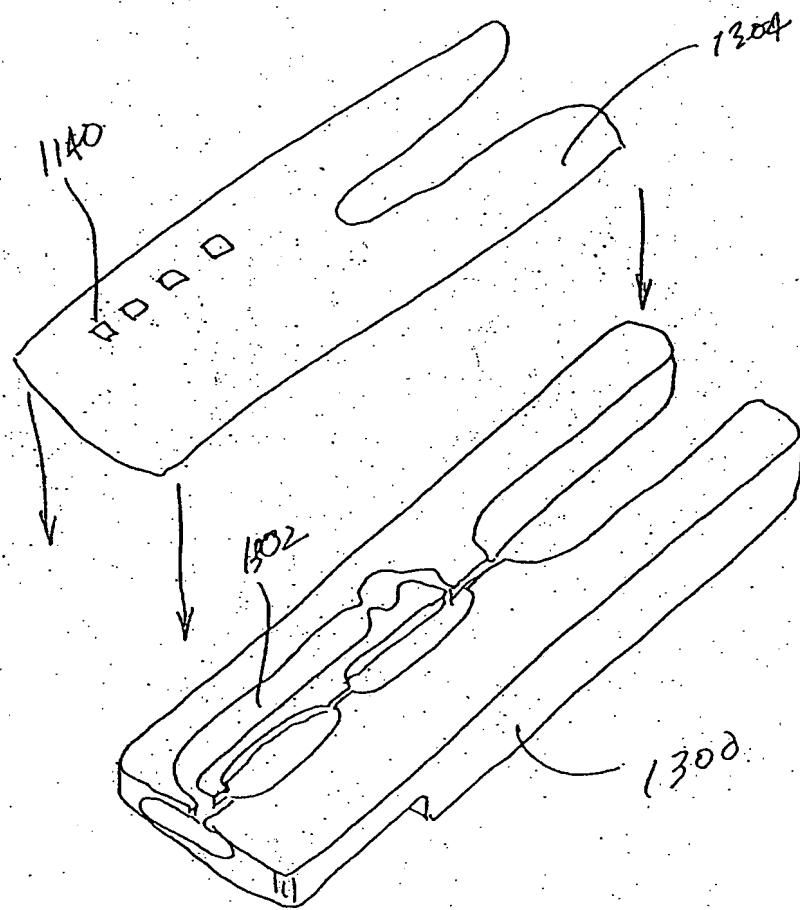
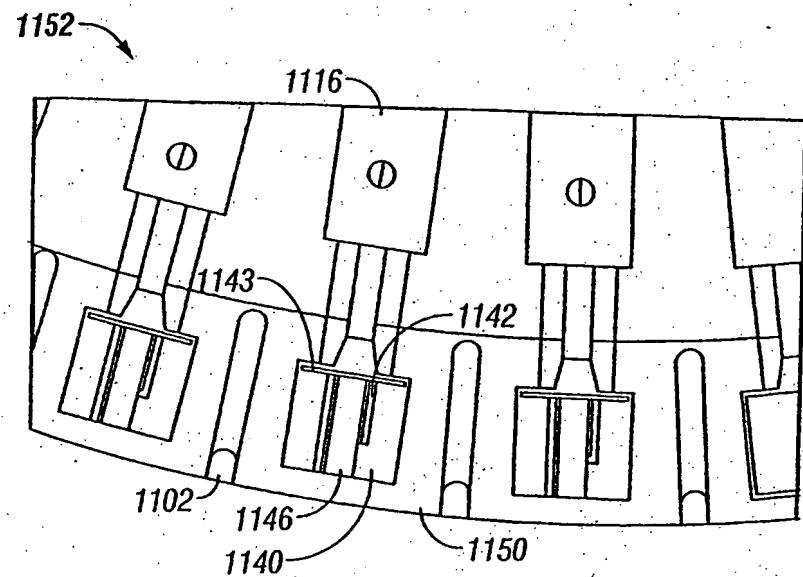


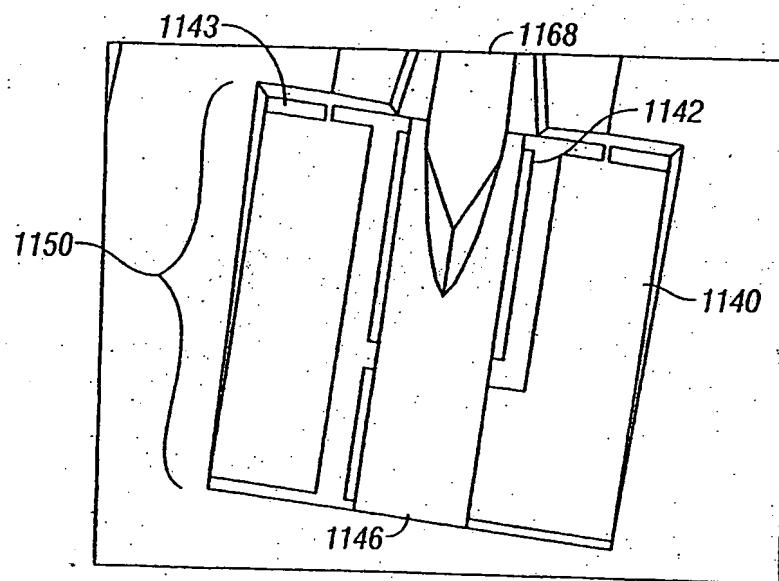
FIG-137



FIG_138



FIG_139



FIG_140

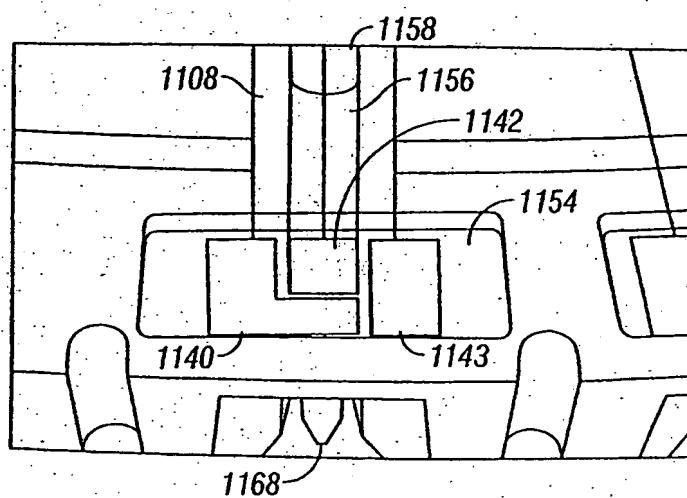


FIG-141

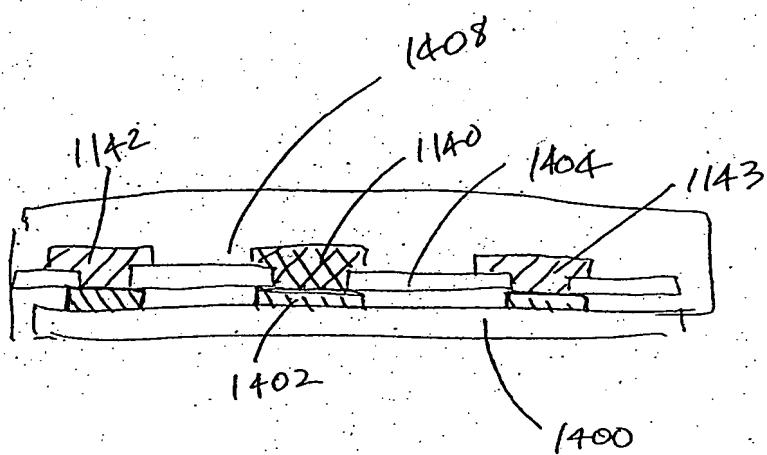
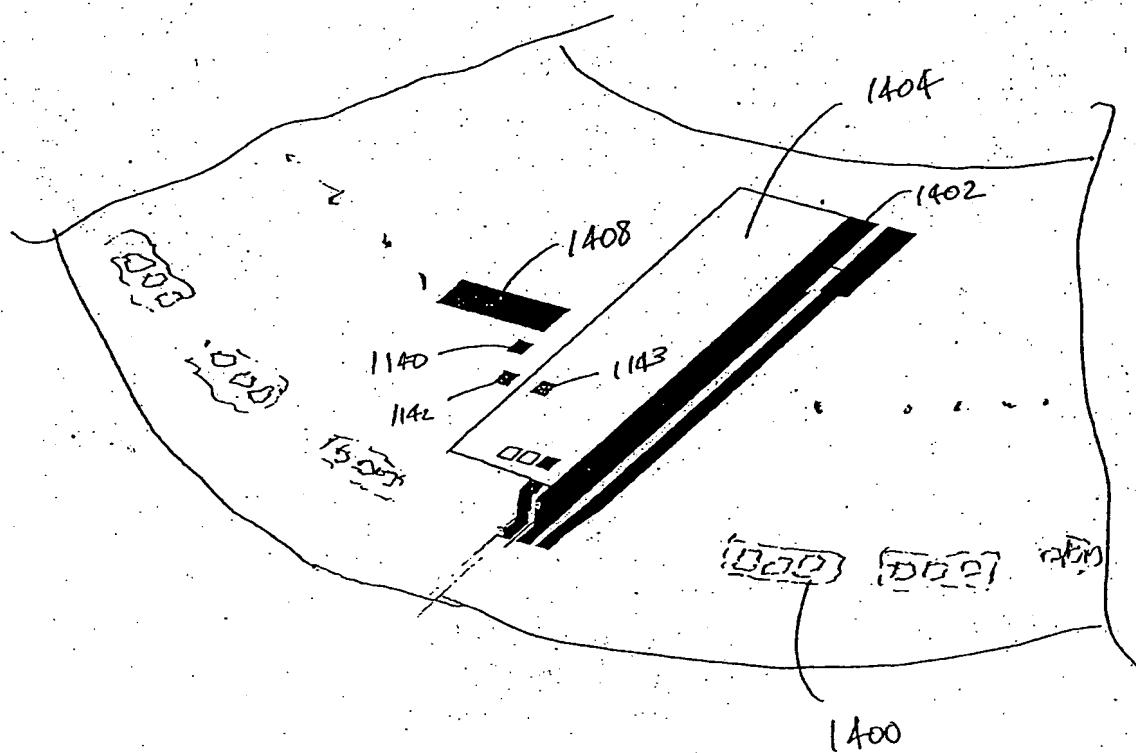


FIG-142



FIG_143

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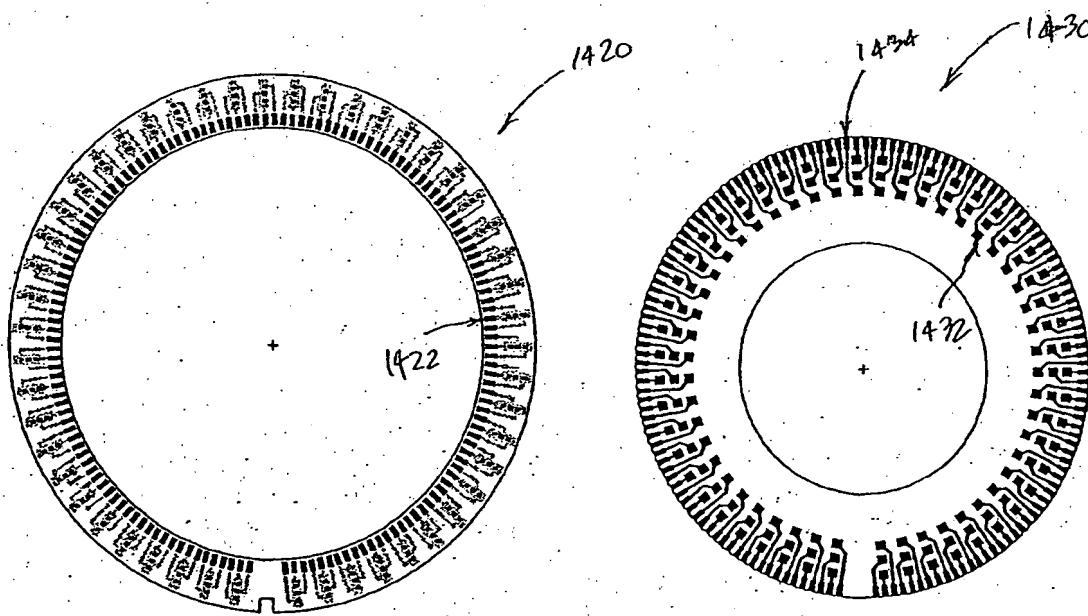


FIG-144

FIG-145

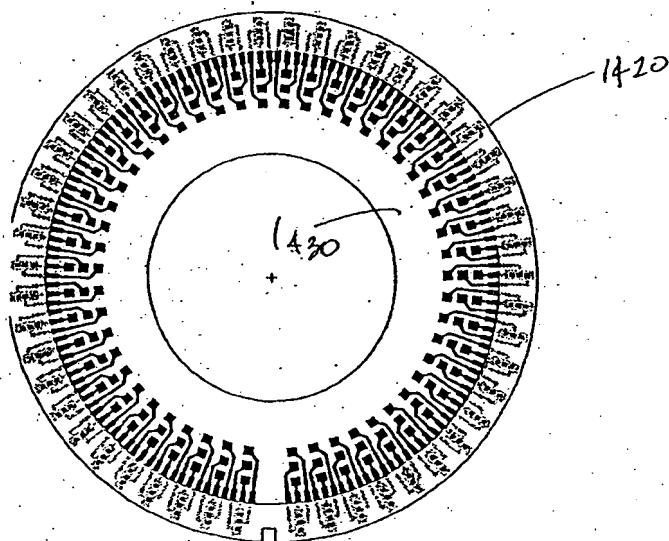
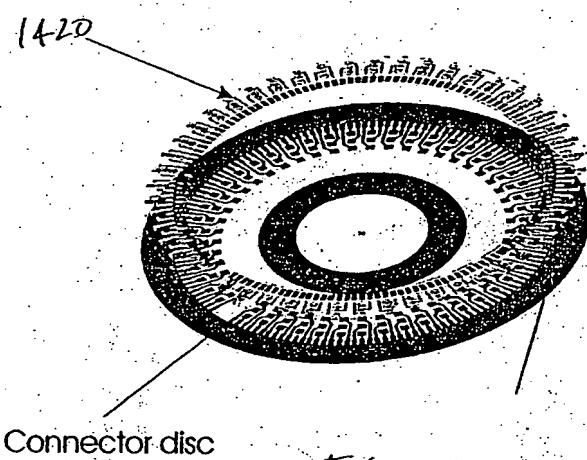
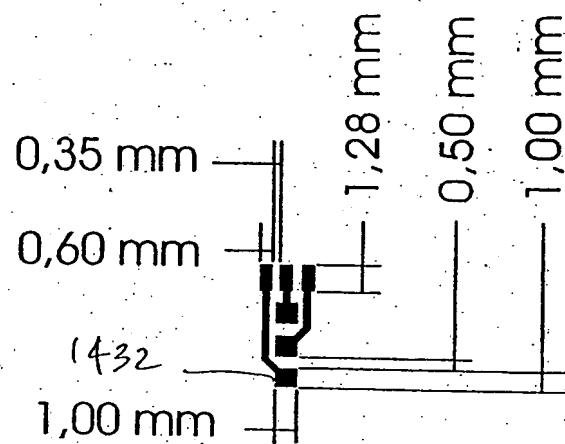


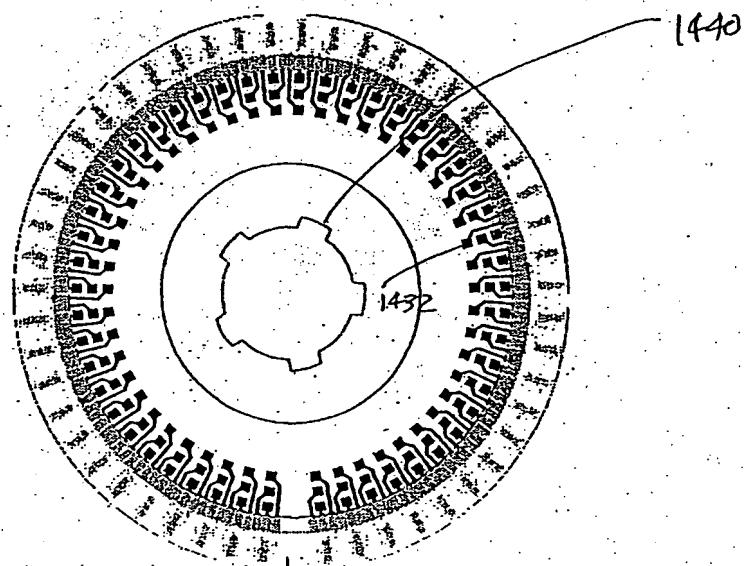
FIG-146



Connector disc

FIG_147

FIG_148
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FIG_149

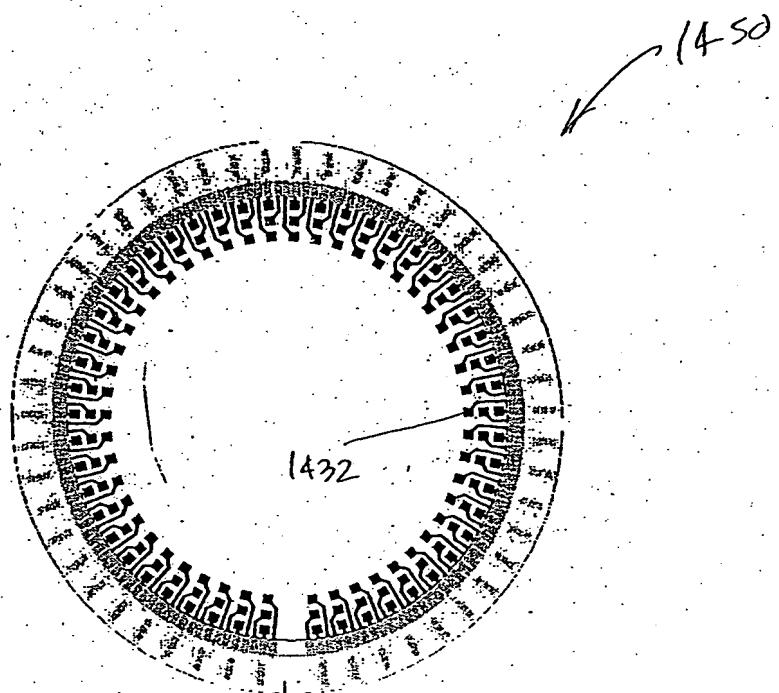


FIG-150

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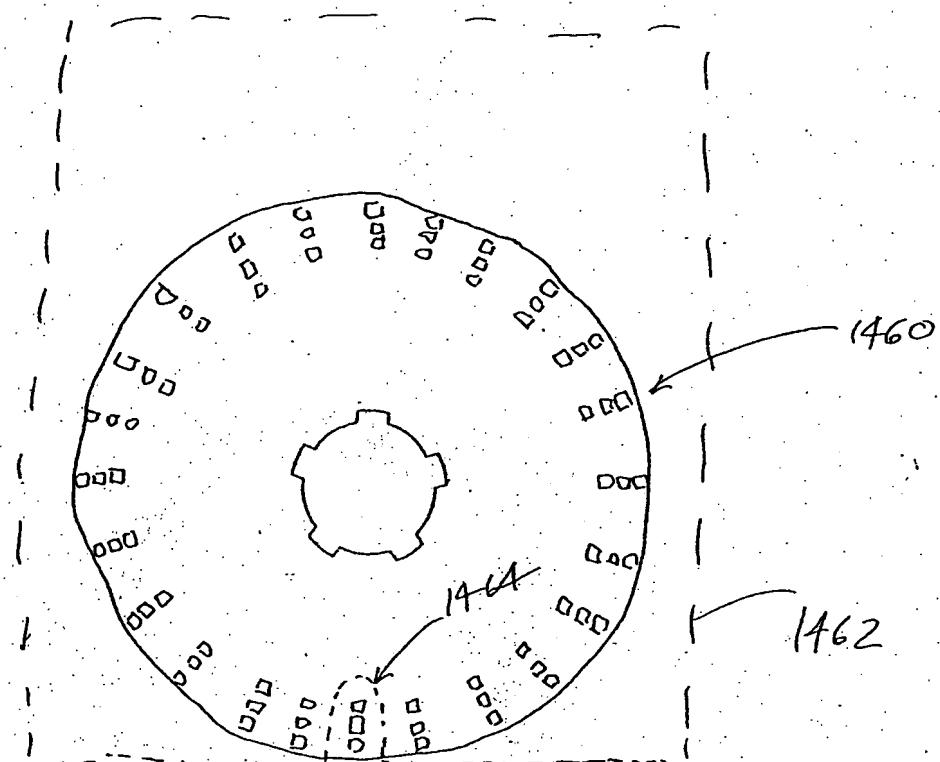


FIG-151

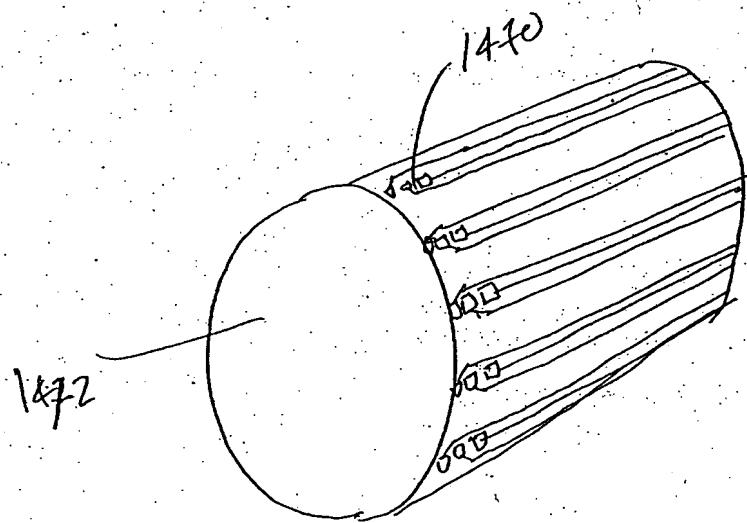


FIG-152

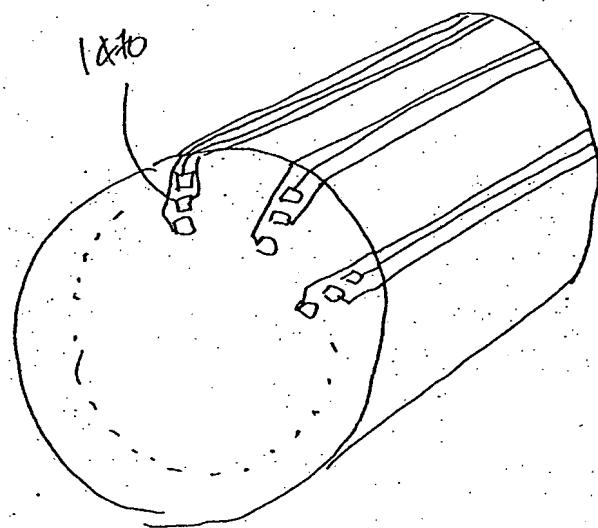


FIG-153

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/40095

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61 B 17/32
US CL : 606/181

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 606/181,182,184,167; 600/573,576,578,583-584

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,206,841 B (Cunningham et al.) 27 March 2001, See entire document.	1-7, 9-11, 17-20 and 22-24
X	US 6,461,496 B (Feldman et al.) 08 October 2002, See entire document.	1 and 19-21
Y		8, 12-16 and 20

<input type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
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Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
18 March 2004 (18.03.2004)	14 APR 2004
Name and mailing address of the ISA/US	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Victor Nguyen